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Platinum Opinion – Collaborative Editorial

Mesh Sling in an Era of Uncertainty: Lessons Learned and the Way Forward

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For many years, synthetic mesh was avoided whenever possible for surgical treatment of stress urinary incontinence (SUI) and/or pelvic organ prolapse (POP) because of the recognized complications of fibrosis and erosion seen with Mersilene [1] and Gore-Tex slings [2].

Petros and Ulmsten [3] in 1990 and Petros and Papadimitriou [4] more recently described a fairly simple procedure with tension-free vaginal tape (TVT), during which the surgeon placed a thin strap of polypropylene mesh in a midurethral position. Since the 1990s, the marketing and use of synthetic materials for SUI and POP indications have dramatically increased. This was particularly noticeable after the publication of a randomized controlled trial comparing TVT with colposuspension [5]. A number of similar procedures were subsequently granted marketing licenses with little clinical data from adequately powered randomized studies. This was followed by a series of modifications including transobturator tape (TOT) [6] and, recently, a wave of single-incision slings, or *mini-slings*, to prevent passage of trocars through the retropubic space or obturator fossa [7]. Concomitantly, the specialty of female pelvic medicine and reconstructive surgery has witnessed the very rapid growth of larger segments of synthetic material, referred to as *mesh*, being implanted beneath the vaginal wall to correct POP based on the early data supporting efficacy of TVT and TOT.

More than 40 implants are on the market [8,9] and are used with little evidence related to mid- and long-term safety and efficacy. Training to place these new implants has often comprised cadaver courses on weekends, review of video procedures, observing "experts" performing implants, and mentorship in institutions by a visiting surgeon. The use of these materials and the surgical techniques have not been limited to subspecialist practice. In 2008, following an escalation in complications reported to the Manufacturer and User Facility Device Experience (MAUDE) database, the US Food and Drug Administration (FDA) issued a first notification to inform the public [8] that these devices and "kits" had risks, should be used with caution, and might result in nonreversible outcomes [10]. A second FDA notification in 2011 sounded even more alarming [11] and provoked a chain reaction from patients, physicians, manufacturers, and lawyers. Similar initiatives were under way in the United Kingdom, with recognition of the problem by the Medicines and Healthcare Products Regulatory Agency (MHRA) [12,13]. As the Internet facilitated connection between desperate patients seeking help [14], television advertisements started to inform the public about issues related to "transvaginal meshes." A number of Web sites inspired by patients' experiences identified problems with mesh (eg, TVT Messed up Mesh [TVT Mum], http://www.tvt-messed-up-mesh.org.uk/).

During specialty meetings, many presentations and discussions have focused on mesh or tape complications and their management, specifically, obstruction, pain, dyspareunia, and erosion that may have irreversible consequences despite multiple interventions [10]. In daily practice, patients have begun to inquire more intensely about "mesh" or "tape," and the regulatory authorities have provided information for patients on this subject. There is a lack of registries to establish the true incidence of the problems with the use of synthetic materials, as has been recognized with the underreporting of these complicated cases to the "optional" MAUDE database [15] and to the other regulatory bodies such as MHRA in the United Kingdom. Although voluntary registries have been established by professional groups, they do not provide accurate information because registration of all cases would be

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required and, invariably, existing voluntary registries are prone to selective reporting of cases.

Existing materials have been introduced on the basis of biocompatibility in the body. Although some initial materials were found to be associated with more problems than others, such as ObTape [16], four groups of biomaterials can be described according to pore size. With recognition of the importance of a pore size of >75 μm between synthetic fibers, it has been suggested that infective problems are reduced [17]. The mechanical properties of meshes have been tested industrially for resistance, pliability, elasticity, and ductile qualities. These properties depend on the type of tissue structure (woven or knitted) and the type of fiber used (mono- and multifilament). With the intention of providing a "silent" material, which does not trigger an unfavorable host-tissue reaction, introducing the foreign body induces a "scarring" response. This fibroblastic reaction replaces the inflammatory reaction, leading to progressive colonization of the prosthesis. It has been suggested that the weave of mesh is important and that open-weave prolene mesh shows unique biomechanical properties, compared with other tested materials, that might lead to reduced erosion rates [18]. Despite these observations, it was reported from the original study by Ward and Hilton that TVT mesh has a significant erosion rate of at least 4% [19]. A number of articles have raised the concern that synthetic materials might not be inert when implanted in the body [20,21].

Finally, as the first awards from individual lawsuits against reputed manufacturers became known, some companies (eg, Ethicon, Bard) decided to no longer market their mesh products. At present, several mesh-focused class-action lawsuits have made the headlines. The first federal litigation was directed at Mentor's ObTape sling and has been settled [16], and the TVT Secur is no longer marketed. Five pelvic-repair-system products from different manufacturers are the subjects of medical device litigation in West Virginia, overseen by Judge Goodwin [22]. Several thousands of petitions are involved in each manufacturer class-action suit. In real-life practice, attorneys often send their clients to centers of expertise for mesh or tape removal and ask for retrieval of the removed parts as evidence for the case. The litigation is against the companies that produce the kits, because the material is defective or the training is improper, as well as the doctors that implant the devices. In this atmosphere, more physicians in the United States are opting for nonmesh treatments (pers. comm., S. Raz, Los Angeles, CA, USA).

Clearly, this litigation process is relatively new, but it is expanding. Advertisements still circulate on a daily basis, and patient referrals for removal of mesh and tape continue to surface everywhere. Credentialing has become a major issue for concerned specialty societies [23], and courses to teach proper technique have intensified. Despite these efforts, it seems that the pendulum is shifting toward renewed scrutiny regarding the broad use of synthetic material in the vaginal wall. Even researchers with established credentials and track records are becoming concerned in light of the recent FDA release dated March 27, 2013, on sling tape for SUI [24] and emerging new scientific data [25].

1. Lessons learned

To be legally marketed, the main prerequisite across the world for a synthetic material is to demonstrate equivalence to existing devices that have been shown to be biocompatible and to go through, for example, the FDA's premarket notification 510(k) process; such processes vary in different parts of the world. However, not all synthetic devices for POP or SUI are equal, and they should not reach the market without being used in carefully controlled clinical studies with adequate safety, efficacy, or adverse outcome data. Postmarket study surveillance (522 orders) on safety and effectiveness has now been mandated in the United States. In Europe this is currently the subject of contemporary discussion, but no similar formal process has been introduced.

Prior to surgery, a patient and her surgeon should have an adequate discussion that includes alternatives, benefits, risks, and complications [12,26,27] (Fig. 1). Surgery for SUI is effective and results in high rates of patient satisfaction [28,29]. Each patient should be offered nonsurgical alternatives, including pelvic floor muscle training. Although these nonsurgical treatments have lower efficacy, an individual patient should participate in her decision based on her own goals and preferences [30]. In addition, when a patient has made the decision to proceed with surgery, alternative surgical options that include non–mesh-based techniques should be offered, such as an autologous fascial sling or bladder neck suspension [31].

Surgeons should perform surgery for SUI or POP only if they are adequately trained in this subspecialist area, perform such surgery on a regular basis, and are aware of all potential therapeutic options. In particular, because complications differ based on the sling technique used, the advantages and the disadvantages should be outlined for each patient prior to final selection of a surgical technique. It is prudent to consider specifically adding the word *mesh* to a surgical consent for mesh-based procedures. In addition, in formulating their procedural recommendations, surgeons may wish to avoid certain risk profiles and consider the feasibility of repeated surgical treatment should the initial sling be unsuccessful. This is important for mesh slings that are placed for treatment and is an even more important discussion when a mesh-based sling is recommended for SUI prophylaxis [32], for which there is less information to inform the discussion of risks and benefits. In the only study to date, approximately six patients would require concomitant treatment during surgery for POP with TVT to prevent one patient from having SUI. Consequently, in our opinion, mesh materials should not be used prophylactically [33].

The evidence in the area of mesh-based slings in surgical practice is evolving rapidly. Surgeons should rely on reputable sources for unbiased information and evidence. In the absence of evidence, mesh-based procedures should be restricted to experimental or research settings until an

RECOMMENDATIONS FOR PATIENTS:

BEFORE SURGERY:

Ask your surgeon about all SUI treatment options, including non-surgical options and surgical options that do and do not use mesh slings. It is important for you to understand why your surgeon may be recommending a particular treatment option to treat your SUI.

Any surgery for SUI may put you at risk for complications, including additional surgery. One complication that may occur when mesh slings are used is vaginal mesh erosion, which could require additional surgery to resolve.

If mesh erosion occurs through the vaginal tissue, it is possible that men may experience penile irritation and/or pain during sexual intercourse.

Ask your surgeon the following questions before you decide to have SUI surgery:

- What surgical or non-surgical treatment options are available and what do you recommend to treat my SUI?
- Have you had specialized training in the surgical treatment of SUI, and if so, what type of training have you had with this particular product and/or procedure?
- What can I expect after surgery and what is the recovery time?
- If I also have pelvic organ prolapse, will that change how you treat my SUI?
- What if the surgery doesn't correct my problem?
- Which side effects should I report to you after the surgery?
- Are you planning to use a mesh sling in my surgery? If so:
  - How often have you performed this surgery using this particular product? What results have your other patients had with this product?
  - What are the pros and cons of using a mesh sling in my particular case? How likely is it that my repair could be successfully performed without using a mesh sling?
  - Are recovery times different for mesh sling surgery compared to non-mesh surgery?
  - Will my partner be able to feel the mesh sling during sexual intercourse?
  - If I have a complication related to the mesh sling, how likely is it that the complication can be resolved? Will you treat it or will I be referred to a specialist experienced with mesh sling complications?
  - Is there patient information that comes with the product, and can I have a copy?

AFTER SURGERY:

Continue with annual check-ups and follow-up care, notifying your health care provider if complications develop, such as persistent vaginal bleeding or discharge, pelvic or groin pain, or pain during sexual intercourse. There is no need to take additional action if you are satisfied with your surgery and are not having complications or symptoms.

If you have complications or other symptoms:
Discuss complications and treatment options with your health care provider. Only your health care provider can give you personalized medical advice.
Consider getting a second opinion from a surgeon who specializes in female pelvic reconstruction if you are not satisfied with your discussion with your health care provider.

Let your health care provider know you have a mesh sling, especially if you plan to have another surgery, plan to become pregnant or have other medical procedures.

If you have had SUI surgery but do not know whether your surgeon used a mesh sling, ask your health care provider.

Talk to your health care provider about any additional questions you may have.

Fig. 1 – Information for patients with stress urinary incontinence. Reproduced with permission of the US Food and Drug Administration [27].

adequate body of information is available to support use in routine practice. Given the rapid adoption of mesh-based SUI procedures with limited long-term follow-up, continued reporting of longitudinal cohorts will be important. Registries should be organized on a national basis in collaboration with professional societies of all relevant disciplines. Such registries may be funded with innovative models of funding that involve industry support on a "per device" model and without any involvement in data collection or evaluation because such registries can be administered independently.

We are lacking an evidence-based approach to managing the wide variety of mesh-based complications. The use of such inclusive registries will allow the evaluation of complication outcomes. Although the clinical experience of subspecialty experts grows daily, stringently designed studies of important questions—for example, incise or excise obstructive mesh slings or use estrogen or excision for minor vaginal tape exposures and the management of erosion into the urinary tract, including the reconstruction of urethral–vaginal fistulae—remain unanswered. Classification of complications to allow comparison of reports [34] will assist research in this area. Significant subspecialty expertise improves the outcomes of such complex cases, and consideration should be given to working with national societies to establish a registry of accredited centers for the functional reconstruction of such complex cases.

2. The way forward

What is the future for use of synthetic material for mesh slings? It behooves all of us to spend a significant amount of time with our patients when considering a tape or mesh placement, along with clear documentation of all risks and known long-term complications and their management [35] (Appendix). In this context, it is essential to outline the other potential therapeutic options that are available. The scientific community has begun to acknowledge how matters can be improved [36] and is looking for solutions to better safeguard the public, including development of a certification process for specialists and "fellow" trainees. In addition, it is likely that the regulatory authorities will adopt more stringent regulations regarding evaluation of new devices before they are introduced into routine clinical practice.

Beyond the current, passionate debates for or against synthetic material, there is limited knowledge about the long-term integration of these devices into the vaginal wall near vital adjacent organs and the risks and benefits of the devices' added strength versus native tissue repair. So, is it the beginning of the end for mesh? This is unlikely because good results can be obtained by experienced hands, as long as patients are adequately informed about the pros and cons of using mesh devices, in particular, complications and lack of adequate long-term data. Certainly it is the beginning of more accountability on the part of physicians, the scientific community, and manufacturers to retain patients' trust and remove residual uncertainties. Future research should be directed at long-term alternatives using tissue-regeneration techniques and absorbable synthetic materials [37].

Conflicts of interest: Christopher R. Chapple is a speaker for Ranbaxy; a consultant for AMS, Lilly, and ONO; and a consultant, researcher, speaker, and trial participant for Allergan, Pfizer, and Recordati. The other authors have nothing to disclose.

Appendix – Take-home messages

- New surgical devices should be adequately assessed before introduction into clinical practice.

- Surgeons should carry out surgery for SUI only if they are adequately trained in the subspecialty and after appropriate evaluation of the patient.
- Although mesh insertion seems like an easy procedure, treating complications of mesh surgery may require extensive and complex procedures.
- Surgeons are not properly informing patients regarding their personal experience, number of cases done, and potential complications.
- Patients are not well informed. Patients should have more access to information about the potential complications of mesh.
- Complications are underreported. The reporting system for patients, physicians, and manufacturers should be improved.
- *Even with complete mesh removal, >30% of patients may be permanently disabled or may experience long-term symptoms.*

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presented 5 cases of urethral and vaginal leiomyoma where diagnosis was made by MRI in all cases prior to surgical removal.[1] This was not the case in our patient. Leiomyoma should be considered in the differential diagnosis of urethral masses.

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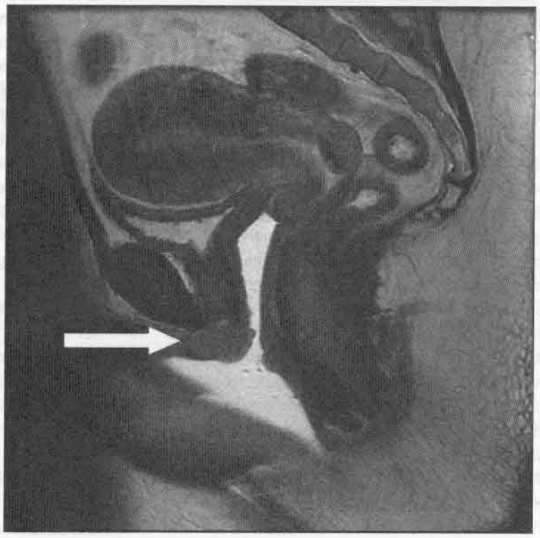

Figure 1: T2-weighted MRI image showing the distal periurethral mass thought to be an infected Skene's gland.

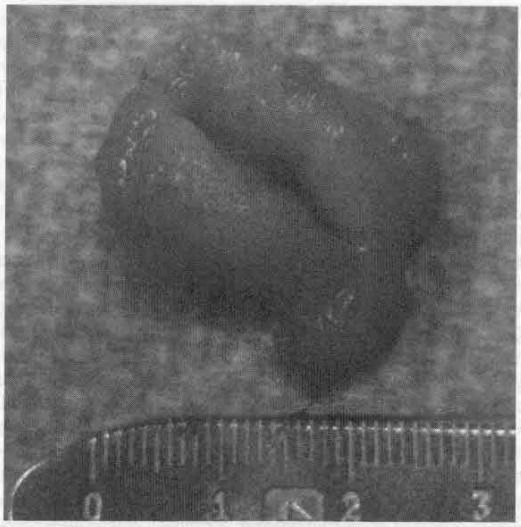

Figure 2: Gross examination of excised solid periurethral mass

Presentation Number: Poster 173

EFFICACY AND SAFETY OF SINGLE INCISION SLING (MINIARC) AFTER FAILED RETROPUBIC AND TRANOBTURATOR MID-URETHRAL SLING PROCEDURES. EXPERIENCE AFTER 12 CASES

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Objectives: To evaluate the efficacy and safety of single incision sling (MINIARC) for the treatment of recurrent or persistent stress urinary incontinence after failed initial retropubic and transobturator mid-urethral slings (TVT, TVT-O, TOT-MONARC, TOT-OBTAPE).

Methods: A retrospective chart review was performed from 2007 to 2011 on 12 patients who had undergone MINIARC or MINIARC-PRECISE procedures for recurrent or persistent stress incontinence after failed initial mid-urethral sling procedures. We assessed uroflowmetry, residual urine volume, urodynamic study, and bladder diary. We evaluated the subjective and objective cure rates, the change of quality of life after the surgery and satisfaction questionnaire. Only one surgeon performed all of the repeat procedures.

Results: Twelve patients underwent repeat mid-urethral single incision sling (MINIARC) procedure after failed initial retropubic (2 cases of TVT) and transobturator (4 cases of TVT-O; 5 cases of TOT-MONARC; 1 case of TOT-OBTAPE) mid-urethral sling procedures performed in other institutions by different providers. Mean ALPP was 82.4±21.0 cmH2O. Mean age was 48 years. Mean follow-up after repeat sling was 22.5 months. Mean duration between initial and repeat procedure was 13.8 months. The overall cure rate was 91.6%. All 12 patients were satisfied with the treatment and 75% of those were "very satisfied". Mean total incontinence quality of life scores improved after repeat single incision sling. All the patients were discharged home the same day. There were no intraoperative or early postoperative complications. There were no cases of erosion or extrusion of the repeat or old sling.

Conclusions: In our patient population, single incision sling (MINIARC or MINIARC-PRECISE) appear to be an effective and safe treatment option for correction of recurrent or persistent stress urinary incontinence after failed initial retropubic and transobturator mid-urethral slings. The subjective cure rate and the satisfaction were high without significant complications.

Disclosures: S. Badalian: Speaker Bureau, Allegran, Consultant, Preceptor, AMS, Speaker Bureau, Warner-Chilcot.

Presentation Number: Poster 174

VAGINAL COLPOPEXY USING A TROCAR-LESS MESH KIT VERSUS TRADITIONAL UTEROSACRAL LIGAMENT SUSPENSION: A RETROSPECTIVE COHORT STUDY

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Objectives: The purpose of this cohort study was to evaluate surgical outcomes after vaginal colpopexy using a commercially-available, trocar-less mesh kit, compared with a traditional uterosacral ligament suspension procedure.

Methods: We included all subjects who underwent a vaginal colpopexy (Boston Scientific Uphold<SUPERSCRIPT>TM NY).

Results: Thirty-two subjects underwent vaginal colpopexy and fifty-five subjects had a uterosacral ligament suspension procedure performed. Women in the vaginal colpopexy group were older (59.8 years vs. 53.1 years, p=0.011) and more likely to be menopausal (87.5% vs. 54.5 %, p=0.002) than those in the uterosacral suspension group but no other significant differences were noted between the two groups. One patient within the vaginal colpopexy group received a postoperative blood transfusion. Three patients (5.5%) in the uterosacral group complained of significant one-sided buttock pain on postoperative day one presumably due to nerve entrapment and required removal of the ipsilateral uterosacral suture. Five subjects (15.6%) in the vaginal colpopexy group complained of transient labial, buttock or groin pain. Three subjects in the uterosacral group had recurrent prolapse requiring sacrocolpopexy compared to zero subjects in the vaginal colpopexy group (5.5% vs. 0.0%, p=0.294). One subject was found to have postoperative mesh exposure in the vaginal colpopexy group which was asymptomatic and successfully treated with topical estrogen cream.

Conclusions: The use of a commercially-available, trocar-less mesh kit to perform a vaginal colpopexy appears to be safe and effective for the treatment of pelvic organ prolapse compared to the traditional uterosacral ligament suspension. Larger randomized trials are warranted to confirm these findings.

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UROGYNECOLOGY

Evaluation and management of complications from synthetic mesh after pelvic reconstructive surgery: a multicenter study

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OBJECTIVE: The purpose of this study was to describe the evaluation and management of synthetic mesh-related complications after surgery for stress urinary incontinence (SUI) and/or pelvic organ prolapse (POP).

STUDY DESIGN: We conducted a multicenter, retrospective analysis of women who attended 4 US tertiary referral centers for evaluation of mesh-related complications after surgery for SUI and/or POP from January 2006 to December 2010. Demographic, clinical, and surgical data were abstracted from the medical record, and complications were classified according to the Expanded Accordion Severity Classification.

RESULTS: Three hundred forty-seven patients sought management of synthetic mesh-related complications over the study period. Index surgeries were performed for the following indications: SUI (sling only), 49.9%; POP (transvaginal mesh [TVM] or sacrocolpopexy only), 25.6%; and SUI + POP (sling + TVM or sacrocolpopexy), 24.2%. Median time to evaluation was 5.8 months (range, 0–65.2). Thirty percent of the patients had dyspareunia; 42.7% of the patients had mesh erosion; and 34.6% of the patients had pelvic pain. Seventy-seven percent of the patients had a grade 3 or 4 (severe) complication. Patients with TVM or sacrocolpopexy were more likely to have mesh erosion and vaginal symptoms compared with sling only. The median number of treatments for mesh complications was 2 (range, 1–9); 60% of the women required ≥2 interventions. Initial treatment intervention was surgical for 49% of subjects. Of those treatments that initially were managed nonsurgically, 59.3% went on to surgical intervention.

CONCLUSION: Most of the women who seek management of synthetic mesh complication after POP or SUI surgery have severe complications that require surgical intervention; a significant proportion require >1 surgical procedure. The pattern of complaints differs by index procedure.

Key words: mesh excision, mesh-related complication, sling, synthetic mesh

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Approximately 11% of women in the United States will require surgical intervention for either pelvic organ prolapse (POP) or stress urinary incontinence (SUI) by age 80 years. Of these women, up to 29% will undergo repeat surgery for symptom recurrence.[1,2] In response to these high recurrence rates, the placement of synthetic mesh during repair is being used increasingly in hopes of achieving more durable improvement.[3] Current evidence suggests that, although the use of such mesh may reduce objective symptom recurrence when compared with native tissue repair only, complications appear to increase.[4-6] Common complications include intraoperative bladder perforation, mesh erosion, chronic pelvic pain, dyspareunia, infection, and fistula formation.[4-16]

How to best balance the potential benefit of improved outcomes with the well-demonstrated risk of repair-related complications remains unclear. The Food and Drug Administration has responded by first issuing a public health warning in October 2008, which was followed by a safety communication in July 2011.[17,18] These warnings highlight the need for a thorough informed consent process but leave the ultimate decision regarding the use of synthetic mesh between clinician and patient. The purpose of this study was to describe the evaluation and management of complications from synthetic mesh after surgery for SUI and POP that were evaluated at 4 US tertiary referral centers. Results were intended to help elucidate the nature of possible complications, the context/circumstances in which they are most likely to occur, and the additional treatment that is typically required for managing these complications.

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TABLE 1
Current Procedural Terminology and *International Classification of Diseases*, 9th Revision, codes used to identify potential subjects

Type of code	Code and explanation
Current Procedural Terminology	57267 Insertion of mesh or other prosthesis for repair of pelvic floor defect
	57295 Revision or removal of prosthetic vaginal graft (vaginal approach)
	57296 Revision or removal of prosthetic vaginal graft (abdominal approach)
	57426 Revision or removal of prosthetic vaginal graft (laparoscopic approach)
	57287 Revision or removal of sling for stress incontinence
International Classification of Diseases, 9th Revision	619.0 Fistula involving female genital tract
	623.2 Vaginal stricture
	625.0 Dyspareunia
	625.5 Pelvic pain syndrome
	625.9 Pelvic pain unspecified
	719.45 Pain, joint, pelvic region
	729.6 Foreign body in soft tissue
	788.20 Retention of urine
	788.21 Incomplete bladder emptying
	936 Foreign body in intestine or colon
	938 Foreign body in alimentary tract
	939.0 Foreign body in bladder or urethra
	939.2 Foreign body vulva or vagina
	939.9 Foreign body in genitourinary tract
	959.9 Foreign body
	996.30 Mechanical complication of genitourinary device implant and graft
	996.65 Infection and inflammatory reaction because of genitourinary device, implant, or graft
	996.76 Mesh erosion
	V58.32 Removal of suture

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Materials and Methods

This was a multicenter, retrospective analysis of all women who attended 4 US tertiary referral centers for evaluation and/or management of a complication that resulted from synthetic mesh placed during surgery for SUI and/or POP. The 4 sites included Cleveland Clinic (Cleveland, OH), The Christ Hospital (Cincinnati, OH), MedStar Washington Hospital Center (Washington, DC), and Women & Infants Hospital of Rhode Island (Providence, RI). All sites obtained individual institutional review board approval.

All sites underwent training to follow standardized data abstraction procedures. To identify potential subjects, a search of the medical/billing records was performed with the use of a uniform set of Current Procedural Terminology and International Classification of Diseases, 9th Revision, codes (Table 1). To reduce irrelevant results, sites were allowed to limit their search to patients of only those practitioners (including both gynecologists and urologists) who were known to have managed vaginal mesh complications. The charts of all potential subjects were screened by site-specific study personnel to determine whether eligibility criteria were met. To qualify for inclusion in the study, the patient had to undergo the index surgery in which synthetic mesh was initially placed on or after Jan. 1, 2006. Selection of this date was intentional because it represents the introduction of vaginal mesh use for treatment of POP and thus allows for a fairer comparison of the proportion of complications that result from the mesh that was used for SUI vs POP. Qualifying index surgeries included the following procedures during which synthetic mesh was placed (cases of biologic mesh use were not considered): (1) midurethral slings, (2) transvaginal mesh, kit or non-kit (TVM), (3) sacrocolpopexies, and (4) any combinations of 1-3. It was not required for the index surgery to have been performed at the study site. Subjects were included if they came to the study site for evaluation and/or management of a mesh-related complication by December 31, 2012, regardless of the type of treatment (eg, inpatient vs outpatient, conservative vs invasive), if any, that had been received at each respective study site.

For all eligible subjects, the following information was collected: demographics, medical history, information about the index surgery, nature of the synthetic mesh complication, management of the synthetic mesh complication, and classification of the mesh complication. Demographic and medical history data included age, race, parity, height, weight, hormonal status, smoking status, and relevant comorbidities (chronic steroid use, diabetes mellitus, and connective tissue disorders). Index surgery data included the date of the index surgery, location (whether it occurred at the study site), indication (SUI, POP, or both), exact procedure, approach, type/brand of synthetic mesh

that was used, and location of synthetic mesh placement. In the event that a patient had multiple procedures with synthetic mesh during the same surgery or had temporally separated surgeries that involved the placement of synthetic mesh, selection of the designated "index surgery" was left to the discretion of the trained study personnel and his/her professional opinion of which procedure was most likely directly related to the resulting complication. All perioperative complications during the index procedure (including bladder injury, bowel injury, hemorrhage, abscess, or other) and any concomitant procedures were also recorded.

The date of first examination at the study site for evaluation/management of the mesh complication and all symptoms were recorded. All management interventions (including observation only, medications, physical therapy, in-office surgery, and/or operating room surgery that required anesthesia) were recorded in chronologic order. If surgery was required for treatment of the complication, details of that treatment surgery, including operating room time, estimated blood loss, and perioperative or postoperative complications that occurred within 6 weeks after surgery were obtained. Posttreatment pain scores at the first follow-up examination that occurred at least 4 weeks after the most invasive intervention and at the last available follow-up examination were also recorded. Finally, the available data were used to classify each patient according to the expanded Accordion classification of general surgical complications, which is a multilevel categorization system that grades postoperative complications by severity and extent of management that includes criteria such as noninvasive vs invasive procedures, organ system failure, anesthesia, and pharmacologic therapy.[19] It is the most widely used postoperative complication classification system across multiple fields of study and is therefore appropriate for the assessment of mesh-related complications.

Study data were collected centrally and managed with the use of REDCap electronic data capture tools that are hosted by the data-coordinating center, Cleveland Clinic. All data were analyzed with JMP software (version 9; SAS Institute Inc, Cary, NC.) All missing data points were treated as missing and not imputed. Many outcomes are descriptive and, accordingly, only appropriate summary statistics were reported. When data are compared across index surgery group types (eg, sling only, TVM with sling, TVM without sling, and sacrocolpopexy with or without sling) pairwise comparisons that always used "sling only" as the reference group were calculated with the χ^2 test (Fisher exact test, 2-tailed).

TABLE 2
Study subject demographics (n = 347)

Variable	Measure
Age at time of index surgery, y[a]	56.6 ± 12.7
Median (range)	56.4 (24.9–91.8)
Race, n (%)[b]	
Non-Hispanic white	226 (65.3)
African American	11 (3.2)
Hispanic	8 (2.3)
Asian	1 (0.3)
Other	7 (2)
Do not know/not recorded	93 (26.9)
Parity, n[c]	2.6 ± 1.24
Median (range)	2 (0–9)
≥1, %	97.9
Body mass index, kg/m^2[d]	28.4 ± 5.3
Median (range)	27.6 (19.3–43.5)
Hormone status, n (%)[b]	
Premenopausal	73 (21.1)
Postmenopausal, do not know hormone replacement status	96 (27.7)
Postmenopausal, not on hormone replacement	104 (30.1)
Postmenopausal, on hormone replacement	40 (11.6)
Do not know/not reported	33 (9.5)
Smoking status, n (%)[b]	
Never	212 (61.3)
Previous	73 (21.1)
Current	43 (12.4)
Do not know/not reported	18 (5.2)
Comorbidities, n (%)[e]	
Chronic steroid use	7 (2)
Diabetes mellitus	23 (6.6)
Connective tissue disease	0

[a] n = 319; [b] n = 346; [c] n = 331; [d] n = 293; [e] n = 347.

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RESULTS

A total of 693 potential subjects across the 4 tertiary referral centers were

TABLE 3
Complaints at evaluation by index surgery type (n = 347)

Complaint	Total, n (%)	Procedure, n (%)				
		Sling only (n = 173)	Transvaginal mesh with sling (n = 76)	Transvaginal mesh without sling (n = 72)	Transvaginal mesh with or without sling combined (n = 148)	Sacral colpopexy with or without sling (8/25 have sling)
Mesh erosion/ exposure/extrusion	148 (42.7)	52 (30.1)	46 (60.5)[a]	35 (48.6)[a]	81 (54.7)	14 (56)[a]
Pain						
Pelvic pain	120 (34.6)	44 (25.4)	29 (38.2)[a]	38 (52.8)[a]	67 (45.3)	9 (36)
Leg pain	9 (2.6)	2 (1.2)	1 (1.3)	5 (6.9)[a]	6 (4.1)	1 (4)
Back pain	9 (2.6)	2 (1.2)	1 (1.3)	6 (8.3)[a]	7 (4.7)	0
Groin pain	14 (4)	4 (2.3)	4 (5.3)	6 (8.3)	10 (6.8)	0
Any type of pain symptom	125 (36)	46 (26.6)	29 (38.2)	40 (55.6)[a]	69 (46.6)	10 (40)
Vaginal						
Dyspareunia	104 (30)	34 (19.7)	35 (46.1)[a]	31 (43.1)[a]	66 (44.6)[b]	4 (16)
Pain to male partner during vaginal intercourse	37 (10.7)	14 (8.1)[11]	13 (17.1)[11]	7 (9.7)	20 (13.5)	3 (12)
Vaginal constriction	15 (4.3)	1 (0.6)	7 (9.2)[a]	6 (8.3)[a]	13 (8.8)	1 (4)
Vaginal discharge	32 (9.2)	8 (4.6)	7 (9.2)	6 (8.3)	13 (8.8)[b]	10 (40)
Vaginal spotting	39 (11.2)	8 (4.6)	16 (21.1)[a]	11 (15.3)[a]	27 (18.2)	4 (16)[a]
Any type of vaginal symptom	160 (46.1)	47 (27.2)	47 (61.8)[a]	46 (63.9)[a]	93 (62.8)	19 (76)[a]
Recurrent symptoms						
Recurrent or de novo prolapse	49 (14.1)	7 (4)	18 (23.7)[a]	22 (30.6)[a]	40 (27.0)[b]	2 (8)
Recurrent or de novo incontinence	87 (25.1)	51 (29.5)	27 (35.5)	6 (8.3)[a]	33 (22.3)	3 (12)
Infection						
Localized/abscess	37 (10.7)	21 (12.1)	4 (5.3)	9 (12.5)	13 (8.8)	3 (12)
Systemic	0	0	0		0	0
Lower urinary tract						
Fistula	6 (1.7)	1 (0.6)	3 (3.9)	2 (2.8)	5 (3.4)	0
Urinary obstruction	66 (19)	56 (32.4)	7 (9.2)[a]	1 (1.4)[a]	8 (5.4)	2 (8)[a]
Voiding dysfunction	98 (28.2)	60 (34.7)	20 (26.3)	15 (20.8)[a]	35 (23.6)	2 (8)[a]
Painful voiding	20 (5.8)	13 (7.5)	3 (3.9)	3 (4.2)	6 (4.1)	0
New onset incontinence	25 (7.2)	3 (1.7)	1 (1.3)	17 (23.6)[a]	18 (12.2)	4 (16)[a]
Other	26 (7.5)	14 (8.1)	5 (6.6)	6 (8.3)	11 (7.4)	1 (4)
Any lower urinary tract symptom	171 (49.3)	96 (55.5)	33 (43.4)	33 (45.8)	66 (44.6)	8 (32)[a]

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TABLE 3
Complaints at evaluation by index surgery type (n = 347) *(continued)*

Complaint	Total, n (%)	Procedure, n (%)				
		Sling only (n = 173)	Transvaginal mesh with sling (n = 76)	Transvaginal mesh without sling (n = 72)	Transvaginal mesh with or without sling combined (n = 148)	Sacral colpopexy with or without sling (8/25 have sling)
Lower gastrointestinal tract						
Fistula	0	0	0	0	0	0
Fecal incontinence	6 (1.7)	1 (0.6)	0	5 (6.9)[a]	5 (3.4)	0
Obstructive defecation/tenesmus	16 (4.6)	2 (1.2)	5 (6.6)[a]	8 (11.1)[a]	13 (8.8)	1 (4)
Painful defecation/ dyschezia	2 (0.6)	0	1 (1.3)	1 (1.4)	2 (1.4)	0
Other	1 (0.3)	0	1 (1.3)	0	1 (0.7)	0
Any lower gastrointestinal symptom	22 (6.3)	3 (1.7)	7 (9.2)[a]	11 (15.3)[a]	18 (12.2)	1 (4)
Nerve injury	5 (1.4)	1 (0.6)	2 (2.6)	0	2 (1.4)	2 (8)
Obturator	1 (0.3)	0	1 (1.3)	0	1 (0.7)	0
Pudendal	1 (0.3)	1 (0.6)	0	0	0	0
Sciatic	1 (0.3)	0	0	0	0	1 (4)
Do not know/ not reported	2 (0.6)	0	1 (1.3)	0	1 (0.7)	1 (4)
Other	0	0	0	0	0	0

[a] Statistically significant difference at $\alpha = .05$ with the use of the χ^2 test (2 × 2 table, Fisher exact test, 2-tailed) that compared transvaginal mesh with sling, transvaginal mesh without sling, and sacral colpopexy each against sling only; [b] Statistically significant difference at $\alpha = .05$ with the use of the χ^2 test (2 × 2 table, Fisher exact test, 2-tailed) that compared transvaginal mesh with or without sling against sacral colpopexy.

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identified with the Current Procedural Terminology and International Classification of Diseases, 9th Revision, codes listed in Table 1. Ultimately, 347 subjects (50.1%) met the eligibility criteria. Baseline demographics of the study population are provided in Table 2. Most patients were postmenopausal, with a mean age of 56.6 ± 12.7 years at the time of the index surgery. The overwhelming majority of the women (97.9%) were multiparous. Only 12.4% of them were known current smokers at the time of their index surgery; 6.6% of them had diabetes mellitus, and 2% of them used chronic steroids for another medical condition.

During the index surgery, 49.9% of the women underwent a procedure for SUI only (ie, sling); 25.6% of the women underwent a procedure for POP only, and 24.2% of the women underwent a procedure for both SUI and POP. Of those who had a POP procedure that involved synthetic mesh, 85.5% procedures were TVM, and 13.9% procedures were sacrocolpopexies. Just over one-half of the study subjects (50.4%) who received evaluation/management of a complication underwent their index surgery at that same study site.

Median time from index surgery to first examination at a participating tertiary referral study site was 5.8 months (range, 0–65.2 months); 25.7% of the women were seen at another facility before being seen at 1 of these sites. The most common complaints were mesh erosion (42.7%), pelvic pain (34.6%), and dyspareunia (30%), although most women (70.3%) had with >1 distinct symptom or complaint (median, 2; range, 0–8). Patients who were seen after TVM or sacrocolpopexies were significantly more likely to have mesh erosion and vaginal symptoms, compared with those who received a sling only (Table 3). Patients with complications after TVM had a significantly higher occurrence of pelvic pain, dyspareunia, vaginal spotting, vaginal constriction, and obstructed defecation than those after sling alone (Table 3). Compared with TVM, patients with complications after sacrocolpopexies were significantly more likely to complain of vaginal discharge but less likely to complain of dyspareunia or recurrent POP (Table 3). Voiding dysfunction was most common in those women who received a sling only (Table 3).

Symptoms were also grouped by severity with the use of the expanded Accordion classification. Overall, 77% of the women had a grade 3 or 4, which is a "severe" complication, according to the Accordion classification (Table 4). Patients whose index surgery involved TVM were significantly more likely to have a grade 4 complication (return to operating room/general anesthesia) than those who received a sling only (Table 4).

The median number of interventions/ treatments for each woman with a

TABLE 4
Complaint severity at evaluation according to the Accordion Expanded Classification[20] by index surgery type (n = 347)

		Procedure, n (%)			
Grade	Total, n (%)	Sling only (n = 173)	TVM with sling (n = 76)	TVM without sling (n = 72)	Sacral colpopexy with or without sling (8/25 have sling)
1[a]	39 (11.2)	27 (15.6)	4 (5.3)[b]	7 (9.7)	1 (4)
2[c]	25 (7.2)	14 (8.1)	2 (2.6)	6 (8.3)	3 (12)
3[d]	52 (15)	37 (21.4)	8 (10.5)[b]	3 (4.2)[b]	4 (16)
4[e]	215 (62)	88 (50.9)	58 (76.3)[b]	51 (70.8)[b]	17 (68)
5[f]/6[g]	0	0	0	0	0
Cannot be classified	16 (4.6)	7 (4)	4 (5.3)	5 (6.9)	0

[a] Mild complication that requires only minor invasive procedures that can be done at the bedside; [b] Statistically significant difference at $\alpha = .05$ with the use of χ^2 test (2×2 table, Fisher exact test, 2-tailed) comparing transvaginal mesh with sling, transvaginal mesh without sling, and sacral colpopexy each against sling only; [c] Moderate complication that requires pharmacologic treatment with drugs other than those allowed for minor complications (antibiotics, blood transfusions, and total parenteral nutrition); [d] Severe complication that requires an endoscopic, interventional procedure or reoperation without general anesthesia; [e] Severe complication that requires management by an operation with general anesthesia; [f] Severe complication: organ system failure; [g] Death.

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complication was 2 (range, 1−9); 60% of the women required ≥2 interventions. The initial treatment intervention was surgical for 49% and nonsurgical for 51%. Of those who initially were treated nonsurgically, 59.3% went on to surgical intervention (3.8% in-office, 90.5% in the operating room, and 5.7% both in-office and operating room). Of the women who initially had an in-office trimming of mesh, 73.3% eventually went to the operating room. The median number of surgeries per patient during the study time period was 1 (range, 0−6); 20.7% of the women required >1 surgery, and 7.8% of the women required >2 surgeries. Compared with sling-only patients, a lower proportion of patients whose index surgery involved TVM with sling underwent medical treatment first. Of the patients who did receive medical treatment, a higher proportion of women with TVM underwent surgery at the study site, compared with sling-only patients (Table 5). For those patients who did undergo surgical intervention in the operating room for treatment of their complication, trimming of mesh/partial mesh excision (area of eroded mesh excised only) was the most common first surgical procedure that was performed (50.9%), whereas complete mesh excision (removal of the entire intravaginal portion of mesh to the lateral arms where they leave the pelvis) was the next most common first procedure (26.9%; Table 6). Complete mesh excision as the first operating room intervention was more common in those who had TVM alone, compared with those that had sling alone (Table 6).

Comment

The purpose of this study was to describe the evaluation and management of complications from synthetic mesh after surgery for SUI and POP at 4 US tertiary referral centers. Several significant trends were noted. First, approximately one-half of the women (49.3%) who sought treatment of a mesh-related complication at a tertiary referral center actually underwent their index procedure at a facility other than that tertiary referral center. This trend has been reported in other studies as well.[12] This raises the potential concern that physicians who perform these mesh procedures may not be aware of the complications their patients experience and that these providers may be responsible for future mesh-related complications with no awareness of the existing magnitude of the issue.

Second, several trends were identified that suggested that the synthetic mesh that is used in the application of slings for the treatment of SUI has a more predictable and less severe course of complications compared with the synthetic mesh that is used for the management of POP. For instance, those patients whose index surgery involved a sling only were significantly less likely to experience an Accordion classification severity grade 4, which is a complication that requires a return to the operating room with general anesthesia, than were those women whose index surgery involved the use of TVM. Furthermore, complications after TVM tend to be more severe, are more chronic in nature, and can be more difficult to treat. For instance, mesh erosion, pelvic pain, dyspareunia, vaginal constriction, vaginal spotting, and obstructive defecation were all significantly more common after an index surgery with TVM than 1 with sling only. Contrarily, urinary obstruction and voiding dysfunction were the only complications that were observed significantly more frequently in those women whose index surgery involved sling only, which suggests that these symptoms may be more related to the actual incontinence procedure rather than the use of mesh for treatment. Additionally, those women with complications after a sling-only procedure were treated more often with medical treatment first and rarely required surgical reintervention. Such findings are important because increased interest in this issue from the Food and Drug Administration potentially threatens the continued use of synthetic mesh in pelvic floor surgery.

Despite the distinction in complication severity between TVM and sling-only procedures, complications that are associated with mesh in general are very concerning. Most patients (60%) received 2 or more unique interventions; even then, there was no guarantee of symptom resolution. Perhaps more surprisingly, 79.3% of all subjects underwent at least 1 surgical intervention, whether in-office or in the operating room. Of those who required any

TABLE 5
Management by index surgery type (n = 347)

Variable	Total, n (%)	Procedure, n (%)			
		Sling only (n = 146)	Transvaginal mesh with sling (n = 76)	Transvaginal mesh without sling (n = 72)	Sacral colpopexy with or without sling (8/25 have sling)
Proportion of women who underwent ≥2 reintervention surgeries	72 (20.1)	34 (23.3)	23 (30.3)	13 (18.1)	2 (8)
Proportion of women who underwent medical treatment first	177 (51)	96 (55.5)	26 (34.2)[a]	36 (50)	18 (72)
Proportion of women who did not undergo any reintervention surgery at study site	72 (20.1)	42 (24.3)	8 (10.5)[a]	17 (23.6)	5 (20)

[a] Statistically significant difference at $\alpha = .05$ with the use of χ^2 test (2 × 2 table, Fisher exact test, 2-tailed) that compared transvaginal mesh with sling, transvaginal mesh without sling, and sacral colpopexy each against sling only.

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surgery, nearly one-quarter of the women (26.2%) required >1 surgery. These results suggest that mesh-related complications that are observed at tertiary referral centers are regularly severe enough to require surgical reintervention. Prospective studies that observe patients from the time of evaluation with complication through their various treatment episodes with measurable outcomes of symptom resolution will be necessary to answer the question of how to best manage various synthetic mesh complications and validate whether the high surgical reintervention rate in this study was justified.

Limitations of this study include its retrospective nature and the biases that are inherent in such an approach. Additionally, the use of coding queries to identify study subjects poses a challenge because not all data are always captured when they should be. Perhaps most importantly, there is no denominator for the total number of patients who underwent an SUI or POP procedure with synthetic mesh. Thus, we can make no comments about the rate at which such complications occur. We can only observe that when they do occur, the nature of the complication is usually severe and often requires surgical intervention. Nonetheless, this information

TABLE 6
Details of first surgical procedure to manage mesh complications

Variable	Total, n (%)[a]	Procedure, n (%)			
		Sling only (n = 128)	Transvaginal mesh with sling (n = 67)	Transvaginal mesh without sling (n = 55)	Sacral colpopexy with or without sling (n = 20)
Trimming of mesh/ partial excision[b]	138 (50.9)	59 (46.1)	37 (55.2)	27 (49.1)	15 (75)[c]
Release of mesh arms[d]	49 (18.1)	19 (14.8)	16 (23.9)	13 (23.7)	1 (5)
Complete mesh excision[e]	73 (26.9)	27 (21.1)	19 (28.4)	24 (43.6)[c]	2 (10)
Recurrent prolapse treatment	63 (23.2)	9 (7)	24 (35.8)	26 (47.3)	4 (20)
Recurrent incontinence treatment	40 (14.8)	14 (10.9)	9 (13.4)	14 (25.5)[c]	3 (15)
Other surgery	56 (20.1)	28 (21.9)	12 (17.9)	12 (21.8)	4 (20)

[a] n = 271; 275 women had surgery, 4 of which were in-office only); [b] Area of eroded mesh only excised[19]; [c] Statistically significant difference at $\alpha = .05$ with the use of χ^2 test (2 × 2 table, Fisher exact test, 2-tailed) that compared transvaginal mesh with sling, transvaginal mesh without sling, and sacral colpopexy each against sling only; [d] Incision made in ≥1 of the lateral mesh arms to release tension; [e] Removal of the entire intravaginal portion of the mesh to the lateral arms where they leave the pelvis.

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is helpful in depicting worst-case scenario outcomes, which can be central to informed consent discussions and decision-making. ■

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Review Article

Management of Mesh Complications after SUI and POP Repair: Review and Analysis of the Current Literature

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Purpose. To evaluate the surgical treatment concepts for the complications related to the implantation of mesh material for urogynecological indications. *Materials and Methods.* A review of the current literature on PubMed was performed. *Results.* Only retrospective studies were detected. The rate of mesh-related complications is about 15–25% and mesh erosion is up to 10% for POP and SUI repair. Mesh explantation is necessary in about 1-2% of patients due to complications. The initial approach appears to be an early surgical treatment with partial or complete mesh resection. Vaginal and endoscopic access for mesh resection is favored. Prior to recurrent surgeries, a careful examination and planning for the operation strategy are crucial. *Conclusions.* The data on the management of mesh complication is scarce. Revisions should be performed by an experienced surgeon and a proper follow-up with prospective documentation is essential for a good outcome.

1. Introduction

Pelvic organ prolapse (POP) affects about 50% of parous women. Approximately, 11% of these women will need surgical correction due to symptoms, like incontinence, voiding dysfunction, and discomfort from vaginal bulge. In the USA, more than 300,000 women undergo surgery for POP annually [1]. Repair with native tissue showed a high recurrence rate up to 30%, especially in the anterior compartment [2]. To reduce the risk of recurrence, transvaginal mesh has been applied in the treatment of POP since the 1990s. In the last decade, the number of mesh operations and various presumed easy-to-use mesh kits from various manufacturers grew exponentially. This development led to a widespread application of this outpatient surgical method. Less attention was paid to possible new complications and only a few clinical trials were available prior to product approval and application. Meshes or grafts potentially add to the complication profile. These include the trauma of insertion, foreign body reaction to the implant in terms of inflammation, infection and/or rejection, contraction of the mesh causing pain, and the stability of the prosthesis over time [3]. In 2008, the U.S. Food and Drug Administration (FDA) issued a warning in dealing with foreign materials for incontinence and POP repair, based on the report of more than 1000 serious side effects by Manufacturer and User Device Experience (MAUDE). Following a systematic review of the literature, the FDA pronounced further examinations on benefits and risks of surgical mesh for SUI (stress urinary incontinence) and POP repair. In September 2011, the FDA organized a scientific advisory board and made 34 manufacturers of POP meshes and 7 manufacturers of SUI meshes perform clinical retrospective studies on their products [4]. Currently, over 30.000 cases due to mesh-related complications and law suits on several manufacturers are brought before the US courts. Reacting to this, several products have been withdrawn from the market by the manufacturers. Despite these developments, in Germany, there are relatively few reactions to the alerts. The changes in the supervision of the medical device approval are currently under debate for the coming EU regulation. In addition to comprehensive education and information of patients on specific mesh-related complications, a special surgical skills training in dealing with foreign materials and the management of possible complications is recommended [5–7].

2. Methods

A systematic review was performed for English language articles published in the last five years from January 2009 to June 2014 in PubMed and the Cochrane Library Database. Search items included the following keywords and phrases: "pelvic organ prolapse and POP," "incontinence," "vaginal surgery," "sacrocolpopexy," "vaginal mesh or implant," "abdominal mesh or implant," "alloplastic material," "Prolift," "Apogee," "Perigee," "Gynemesh," "Gore-Tex," "complications," "vaginal or endoscopic or laparoscopic or abdominal resection," and "explantation." Keywords appeared in the title, abstract, or both. Studies with more than 10 reported complications after mesh application for POP or SUI were included. Studies with lacking information on primary surgery, complications, and management were excluded. Classification, risk factors, and treatment concepts of complications after mesh implantation were analyzed. The primary outcomes assessed were the subjective (patient-reported) and objective cure/improvement rates. Secondary outcomes included reoperations for complications and recurrent incontinence after the initial treatment. Data were analysed using RevMan v.5.3 (Cochrane Collaboration, Oxford, UK) and GraphPad Prism v.6 (Graphpad Software, Inc.). Quantitative synthesis was done when more than one eligible study was identified. The outcome results were expressed as weighted means difference (WMD), standard deviations (SDs), and risk ratio (RRs) with 95% confidence intervals (CIs) for dichotomous variables using the Mantel-Haenszel method [8]. Methodological heterogeneity was assessed during selection, and statistical heterogeneity was measured using the chi-square test and I^2 scores. A random effects model was used throughout to reduce the effect of statistical heterogeneity [9]. Treatment failure risk was defined as reoperation after the initial treatment.

3. Results and Discussion

No randomized trials on the surgical treatment of mesh complications were detected. Only one was a partly prospective trial on mesh resection [10]. A total of 17 retrospective studies were included in the review (Table 1). Different conservative approaches and surgical techniques for the resection of alloplastic materials after the treatment of pelvic organ prolapse and stress urinary incontinence are presented. Initial surgeries were midurethral sling (MUS), transvaginal mesh, and abdominal colposacropexy. Only alloplastic polypropylene materials were used.

3.1. Classification of Complications. To analyze the mesh-related complications, a Clavien-Dindo classification of surgical operations is often used in the literature [11]. The advantages hereby are a clear correlation to the management of complications and broad acceptance. However, the information on the site and timing of complications is missing. In addition, the classification is not always adequate; for example, the clinically less severe intraoperative bladder injuries must be classified as Grade III complications and distort the analysis. International Continence Society (ICS) and International Urogynecologic Association (IUGA) introduced in 2010 a consensus-based standardized terminology and classification for the description and documentation of specific complications after the use of implants in pelvic floor surgery of women [3]. The classification is based on the information on the category, time, and location of complications. Because of high complexity and low concordance in different trials, the ICS/IUGA classification is currently rarely used [6, 12]. However, the classification could be valuable for the reporting of long-term data in registries.

3.2. Complications and Risk Factors. Polypropylene meshes are usually used for vaginal repair of POP and SUI. The overall rate of mesh-related complications after transvaginal mesh application for POP is about 15–25% and mesh erosion is up to 10% for these indications [6, 13]. The most common complications (retrospective review of 388 cases with complications) after implantation of midurethral sling (MUS) are overactive bladder (52%), obstructive micturition (45%), SUI (26%), vaginal mesh exposure (18%), chronic pelvic pain (14%), local infection (12%), dyspareunia (6%), and vesicovaginal fistula (4%) ([14], Table 2). Kasyan et al. analyzed the biggest series of 152 complications (22.5%) following Prolift transvaginal mesh for POP. The following complications were detected: erosions (21%), dyspareunia (11%), mesh shrinkage (4.4%), pelvic abscess (2.7%), and fistula (1.3%). Younger age, less prominent prolapse, hematomas, and concomitant hysterectomies were associated with higher risk of complications [15]. As part of the abdominal sacrocolpopexy where nonabsorbable synthetic materials (Mersilene, Prolene, Polypropylene, Gore-Tex) are applied, the risk for mesh erosion is between 0 and 12% (medium risk 4%). Causes of complications were primarily surgical techniques, concomitant surgeries, non-type 1 meshes, and previous surgery in the field [6, 7, 16]. Most complications occur in a time range of one to five years after the operation [12]. Median time to revision in selected trials was 19.2 mos (5.8–59). The complications are attributed to a considerable extent to the wrong indication, faulty surgical techniques (tape positioning and overcorrection), and material properties (biocompatibility and contraction of the mesh material). New developments in material optimization are currently expected. Other risk factors retrieved from multivariate analysis were previous anti-incontinence procedure, obesity, and estrogen status [5, 6, 15]. Reasons for vaginal mesh exposure of the mesh material are categorized into tissue causes and biomechanical mesh properties. Tissue causes include superficial placement, traumatic dissection, tissue healing, and thin and atrophic vaginal mucosa, especially in postmenopausal women [16].

3.3. Management Strategies for Mesh Complications. The current retrospective data on mesh excision for complications is presented in Table 1. 12 trials reported on complications after MUS, 8 trials on complications after transvaginal mesh for POP repair, and 3 trials on abdominal colposacropexy. Median patient number in the studies was 42 patients (8–347). Mean follow-up after the treatment of mesh-related complications was 22.6 mos (6 weeks–65 mos). Many authors propagate an initial conservative approach with antibiotics

Table 1: Studies on management of mesh related complications after incontinence and prolapse surgeries.

Author	Trial	Number of patients	Mesh	Complications	Median time to revision	Management	Concomitant procedure	Follow-up
Abbot et al. 2014 [17]	RT	347 (49.9% MUS; 25.6% TVM or CSP; 24.2% combination)	Various	30% dyspareunia 42.7% mesh erosion 34.6% pelvic pain 77% grade 3 or 4 (reoperation) complication	5.8 mos (0–65.2 mos)	(1) Trimming of mesh/partial excision (50.9%) (2) Release of mesh arms (18.1%) (3) Complete intravaginal mesh excision (26.9%) (4) Recurrent prolapse treatment (23.2%) (5) Recurrent incontinence treatment (14.8%) (6) Other surgeries (20.1%) (7) Initial conservative treatment (23%) 60% ≥2 interventions	MUS	
Agnew et al. 2012 [18]	RT	63 MUS	Various synthetics (67% monofilament TVT, 17% TOT)	100% voiding dysfunction	12.4 mos (1 week–8 yrs)	(1) Simple sling division (73%) (2) Partial excision of sling (21%) (3) Concomitant procedure to prevent Re-SUI (4/63)	Burch, MUS	Persistent voiding dysfunction (1) 10.9%; (2) 7.7%; (3) 50% ($P = 0.09$) Subsequent surgery for recurrent SUI (1) 2.2%; (2) 23.1%; (3) 0% ($P = 0.04$) De novo urgency (1) 10.9%; (2) 15.4%; (3) 25% ($P = 0.51$)
Blaivas et al. 2013 [19]	RT	47 MUS	Type 1 76% Types 2–3 23%	OAB (70%) SUI (55%) Recurrent UTI (21%) Pelvic pain/dysuria (34%) Obstructive symptoms (9%) Vaginal extrusion (9%)	2 yrs (1 mos–8 yrs)	(1) Sling excision + urethrolysis (34%) (2) Sling excision + urethral reconstruction (including fistula repair) + autologous fascial sling (30%) (3) Sling incision (21%) (4) Partial cystectomy (10%) (5) Ureteroneocystostomy (4%)	MUS	2 yrs (0.25–12 yrs) Successful treatment 72% 28% recurrent surgery refractory pain (19%), mesh extrusion (17%), and OAB (8%)
Costantini et al. 2011 [20]	RT	12 (12/179, 6.7%) mesh erosion after abdominal CSP	11 PP, 1 Gore-Tex	100% mesh erosion 41% vaginal bleeding 33% asymptomatic 17% dyspareunia 17% infection (1x Gore-Tex)	22.9 mos (2–66 mos)	(1) Antibiotics and local estrogen (100%) (2) Vaginal (partial) mesh resection (83%) (3) Abdominal resection (17%) (4) Endoscopic (8%)		57 mos (18–120 mos) (1) All needed surgery (3) Recurrent cystocele (4) Fistula, abdominal revision
Davis et al. 2012 [21]	RT	12 TVT	PP	100% mesh erosion	59 mos (7–144 mos)	Endoscopic holmium: YAG laser excision (100%)		65.5 mos (6–134 mos) 33% second laser excision 17% surgery for recurrent SUI 8% (1 patient) abdominal mesh resection
Firoozi et al. 2012 [22]	RT	23 TVM for POP	Various PP	Vaginal/pelvic pain (39%), dyspareunia (39%), vaginal mesh extrusion/exposure (26%), urinary incontinence (35%), recurrent pelvic organ prolapse (22%), bladder mesh perforation (22%), rectal mesh perforation (4%), ureteral perforation injury (4%), and vesicovaginal fistula (9%)	10 mos (1–27 mos)	(1) Transvaginal excision (90%) (2) Transvaginal/endoscopic (5%) (3) Transrectal/transperineal (5%) (4) Concomitant POP/SUI repair (45%)	TVM, MUS	3 mos 14% UTI 4.3% collagen injection for Re-SUI 4.3% PFT for perineal pain
Greiman and Kielb 2012 [23]	RT	28 (28/118, 23%) MUS	PP	Intravesical sling (4%), extruded vaginal mesh (93%), obstructive voiding symptoms (78%), dyspareunia (42%), and vaginal bleeding (21%)	15 mos	(1) Sling loosening, incision in the midline (2) If mesh erosion >1 cm a resection		11% reoperation for mesh extrusion, no other complications
Hammett et al. 2014 [24]	RT	57 patients (26 MUS, 23 TVM, and 9 intraperitoneal prolapse CSP)	Various PP	100% mesh erosion with pelvic pain (55.9%), dyspareunia (54.4%), and vaginal discharge (30.9%).		(1) Vaginal mesh excision (91%) (2) Abdominal resection (all CSP, $n = 9/15$, 40%)		6 weeks 57% symptoms completely resolved 12% required more than 1 surgery for mesh excision (1) 9% UTI (2) 4.5% cardiopulmonal complications; 18% sepsis; 45% wound infection

Table 1: Continued.

Author	Trial	Number of patients	Mesh	Complications	Median time to revision	Management	Concomitant procedure	Follow-up
Hampel et al. 2009 [25]	RT	48 MUS (44 TVT, 4 TOT)	Various PP	De novo urge (65%), mesh erosion (21%), dyspareunia (19%), UTI (35%), and fistula (6%)		(1) Partial mesh resection (trans-/suburethral, 23%) (2) Self-catheterisation (23%) (3) Botox/neuromodulation (27%) (4) Fascia plastic (10%) (5) Complete abdominal-vaginal mesh resection (8%) (6) Urinary diversion (2%) (7) Fistula repair (6%) (8) Conservative treatment (25%)		42% symptoms completely resolved
Kasyan et al. 2014 [15]	RT	152 TVM	Prolift (Gynecare), PP	Erosions (21%), dyspareunia (11%), mesh shrinkage (4.4%), pelvic abscess (2.7%), and fistula (1.3%)		(1) Conservative treatment with local oestrogen (2) Partial/total mesh excision		
Nguyen et al. 2012 [26]	RT	82 MUS (2.2%)	Various			(1) Sling loosening or transaction for voiding dysfunction (60%) (2) Excision for vaginal mesh exposure 30 (36%) (3) Excision for pain (1.2%) (4) Excision for urethral erosion (1.2%) (5) Drainage of retropubic hematoma (1.2%)	MUS, colporrhaphy, and CSP	
Abdel-Fattah et al. 2006 [16]	RT	34 TVM (2.2%)	Various			(1) Excision for vaginal mesh exposure (85%) (2) Excision of vaginal suture (6%) (3) Biologic graft reoperation (12%) (4) Drainage hematoma/abscess (6%) (5) Bowel resection for obstruction (3%)		
Padmanabhan et al. 2012 [27]	RT	85 (MUS, TVM)	Various PP	Perforation of urethra (14%), bladder (36%), and vagina (50%)		(1) Vaginal excision (14%) (2) Lower urinary tract excision (47%) (3) Partial cystectomy (21%) (4) Urethroplasty (21%)		Subjective cure in 75% and improvement in 21% SUI (6.6–12.5%)
Renezeder et al. 2011 [28]	RT	118 (80% MUS, 20% TVM)	Various PP (88% type 1)	De novo urgency (46.6%), dyspareunia (41.5%), recurrent UTI (39.0%), mesh erosion (37%), and vaginal bleeding (9.3%)	27 mos (1–89 mos)	(1) Tissue patch covering (17.8%) (2) Partial removal (65.3%) (3) Complete removal per laparotomy (12.7%) (4) Bone stabilization (0.8%) (5) Excision of granulation tissue (3.4%)		8 weeks 45.5% urgency
Ridgeway et al. 2008 [29]	RT	19 TVM	Monofilament PP	Chronic pain (31%), dyspareunia (31%), recurrent pelvic organ prolapse (42%), mesh erosion (63%), and vesicovaginal fistula (16%)		Partial tailored vaginal mesh resection with concomitant procedures	Burch, MUS	33 weeks (16–75 weeks) 16% UTI 5% hematoma 21% persistent symptoms
Rouprêt et al. 2010 [30]	RT	38 TVT	PP	Mesh erosion/extrusion (42%), pelvic pain (39%), and obstruction (18%)		(1) Laparoscopic (97%) (2) Laparoscopic + vaginal (3%)		38 mos (2–80) Healing and pain release (100%) Recurrent SUI (66%)
Shah et al. 2013 [31]	RT	21 MUS	Polypropylene, type I	Urethral perforation (67%), bladder perforation (33%), fistula (19%), vaginal pain (67%), urgency (29%), incontinence (38%), obstruction (33%), dyspareunia (19%), and hematuria (24%)	15.5 mos (1–60 mos)	(near) Total mesh excision, urinary tract reconstruction, and concomitant pubovaginal sling with autologous rectus fascia	MUS, urethroplasty	22 mos (6–98 mos) Continence (81%) Incisional seroma (9.5%) Additional procedures (36%) UTI (9.5%) Pelvic pain (9.5%) dyspareunia 9.5%

RT: retrospective trial; PT: prospective trial; MUS: midurethral sling; TVM: transvaginal mesh; TVT: tension-free vaginal tape; TOT: transobturator tape; CSP: colposacropexy; PP: polypropylene.

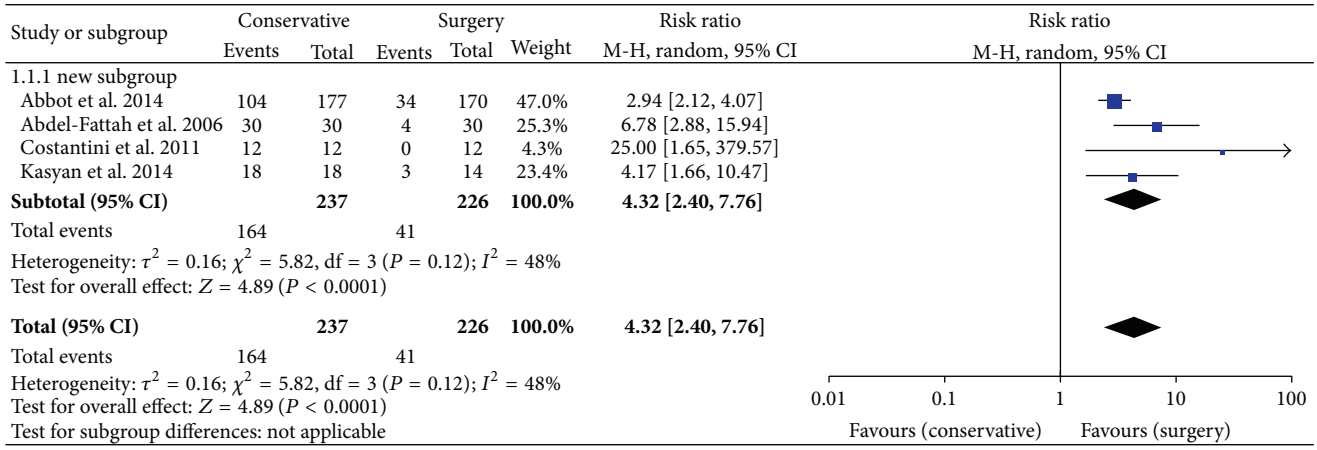

Figure 1: Treatment failure risk for mesh-related complication after conservative treatment versus mesh excision. CI: confidence interval; M-H: Mantel-Haenszel [15–17, 20].

Table 2: Complications of midurethral slings (total number: 388 women sent for revision) [14].

Complications	Number	Percentage
Overactive bladder	201	51.8%
Lower urinary tract obstruction	173	44.58%
Recurrence of SUI	101	26.03%
Vaginal exposure	68	17.52%
Pain	54	13.91%
Infective complications	48	12.37%
Dyspareunia	22	5.67%
Vesicovaginal fistula	14	3.6%
Inrolled sling or contraction of material	18	4.63%
Intraoperative bladder injury	11	2.83%
Groin/upper thigh pain	11	2.83%
Postoperative hematoma	10	2.57%
Bladder/urethral penetration	18	4.63%
Foreign body sensation in vagina	6	1.54%
Husband's penis laceration	6	1.54%
Groin infection	4	1.03%
Necrotizing fasciitis	3	0.77%
Retropubic abscess	3	0.77%
Urethrovaginal fistula	2	0.51%
Intraoperative bowel injury	1	0.25%

and local estrogen application in cases of mesh erosion. However, new studies show an advantage of the timely revision surgery to relieve the symptoms. The analysis of trials comparing conservative treatment with surgery for mesh erosions showed a 4.32-fold risk ratio for treatment failure after the conservative approach (Figure 1). Abbott and colleagues showed that 60% of the initially conservatively treated patients required surgical intervention and 60% of the total cohort were operated on at least twice [17]. Erosions in the vagina or internal organs with consecutive infection, pain, dys- or hispareunia, voiding dysfunction due to obstruction, and urge incontinence often require surgical revision [25]. In

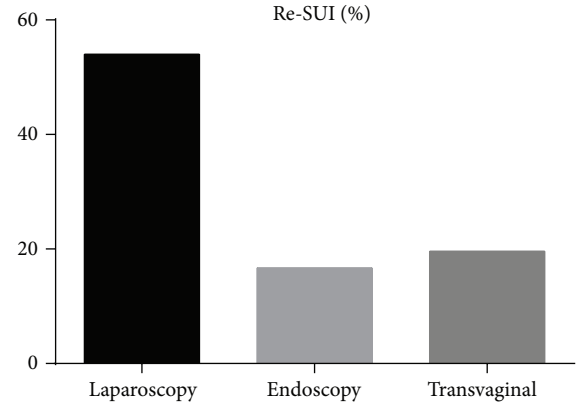

Figure 2: Recurrent incontinence after MUS-mesh excision (mean), $P < 0.05$.

the current US-American and European studies with long-term observation, the rate of postoperative mesh explantations was about 1% after a midurethral sling (MUS) and about 3% after a vaginal mesh for POP repair [26, 32]. The complications can be often corrected by mesh resection, but, in some cases, further surgeries for de novo incontinence (10–25%) or POP (7–47%) were necessary [17]. Figure 2 shows the percentage of recurrent stress incontinence depending on different MUS-excision techniques. Laparoscopic abdominal resection causes a 3-fold higher risk of Re-SUI probably due to a complete incision and excision of the mesh arms [30]. The result was however not significant due to a small trial number. There are a few data on the effect of mesh explantation on dyspareunia and chronic pelvic pain. Previous studies suggest that the pain due to the scarring and foreign body reaction may persist even after the mesh removal [33].

A comprehensive diagnosis of symptoms and localization of erosion by cystoscopy, vaginal examination, imaging and urodynamics, education of patients on possible irreversible damage, and careful planning of the operation steps are required prior to revision surgery. A careful clinical examination and determination of the pain location by trigger

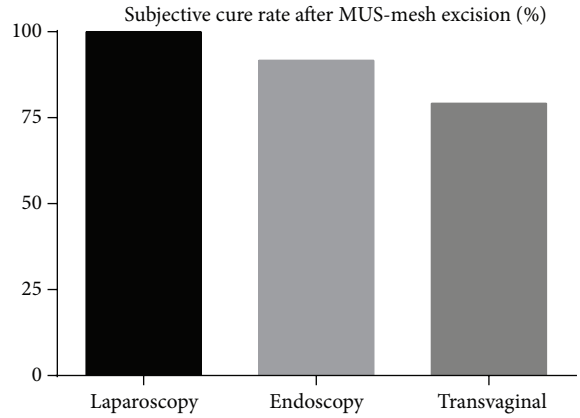

Figure 3: Subjective cure rate after MUS-mesh excision (mean), $P < 0.05$.

points are excellent markers for planning of the site and extent of mesh resection [20, 33]. However, a standardized surgical procedure and access do not exist up to date. The analysis of the available studies showed a similar subjective cure rate of 79–100% for different techniques (Figure 3). The rate of reoperations was higher if an endoscopic or transvaginal access were chosen [18, 19, 21, 22, 24, 30]. However, the hospital stay, operation time, and postoperative pain were higher in the case of laparoscopic mesh excision [30]. Generally, a vaginal access with partial or complete resection of the infected foreign material is favored in most trials (88% of the analysed studies). Non-type 1 alloplastic materials according to Amid classification (e.g., polytetrafluoroethylene and Gore-Tex) have to be removed completely in case of erosion or infection in order to achieve symptom relief [34]. A complete mesh excision can be very difficult especially for abdominal access. Complications such as bleeding, fistula, neuropathies, and prolapse recurrence are frequent [20]. Different transvaginal techniques like sling loosening, mesh incision, and partial or complete excision were described in included studies but no clear strategy or algorithm could be found (Table 1). Costantini and colleagues propose the following intraoperative management of mesh exposure: closure of the vaginal defect with double-layer suture to avoid a direct mesh contact with the mucous membranes, flush with antibiotic solution, no stitching of the full thickness of the vaginal wall, atraumatic preparation, use of nonwoven, nonabsorbable suture and polypropylene meshes, avoidance of concomitant hysterectomy, and long-term follow-up after the revision [20]. Similar vaginal techniques with optional excision of the alloplastic material and two-layer closure of a vesicovaginal fistula are described by other authors [22]. The German group from Mainz University reported on the urogynecological management of complications based on 259 patients after implantation of MUS [25]. In the case of de novo OAB, the symptoms improved only after the resection of the portion of the sling which was in contact with the urethra. The wrong position of the sling could be detected by pelvic floor sonography (PFS). PFS is an important tool to assess the tape position, form, and distance from urethra. The reasons for the complications and sling failure can be identified and corrected. The ultrasonography evaluation of a well-positioned sling provides certainty that a success of conservative therapy can be expected. In case of a dystopic position of the sling, the first step is to evaluate the sling location and to decide whether or not the band can be saved [34]. The removal of the foreign material was more difficult if the initial operation has been long ago. Particularly difficult and traumatic for the pelvic floor were the excisions of transobturator tapes [25]. Infections of the alloplastic material in the obturator fossa are especially dangerous for the development of abscesses or necrotising fasciitis and require careful debridement and follow-up. If a significant erosion of the mesh was diagnosed, partial vaginal material removal has been usually performed. In case of vaginal mesh exposure (small erosions under 1 cm without infection), the defect could be closed by a suture. In case of mesh shrinkage, a resection of the fibrotic band in the paravaginal sulci was proposed. In some cases, infection of TOT required extensive debridement with opening of the deep tissues of the groin and adductor compartment, removal of the complete tape, antibiotics, and sometimes hyperbaric oxygen therapy [15]. Agnew and colleagues reviewed 63 women with voiding dysfunction (>150 mL residual volume) after MUS (67% TVT). Three different surgical procedures were analysed (simple sling division, partial resection, and concomitant SUI procedure). Taking into account the results of the findings (Table 1), the authors changed their strategy to divide synthetic midurethral slings lateral to the urethra and then carefully perform cystourethroscopy to ensure that no urinary tract injury has occurred [18].

A tertiary center in the US presented retrospective data on 47 women after salvage operation following at least one revision on mesh-related complications. Different operative strategies and approaches were applied, depending on the intraoperative findings. The median follow-up was 2 years. Patients presented with various symptoms and 72% could be treated successfully (QoL questionnaire) by the first salvage operation. However, 14 women needed a reconstruction of the urethra, 5 women a continent stoma, and 2 women a partial cystectomy. The treatment of patients with symptoms of chronic pain was difficult; only 28% reported a relief of symptoms postoperatively. The authors assume 3 potential causes of mesh-related urethral complications; namely, (1) the surgeon simply pulls the sling too tight at surgery, (2) a correctly placed sling contracts with time due to tissue ingrowth, and (3) faulty surgical technique results in placement of the sling directly into the urinary tract [19].

Other case reports showed good postoperative results after covering the exposed alloplastic material with vulvar fat without resection [35]. In case of sling erosion into the bladder with consecutive infections, stone formation, and pain, transurethral resection or laser excision (holmium and thulium) techniques have been successful [21, 36]. Other groups reported successful individual cases with laparoscopic and robot-assisted excision and transvesical reconstructions to treat the mesh erosions after MUS implantation [30, 37, 38].

4. Conclusion

Mesh-related complications are a current emerging problem, which confronts all urologists and gynecologists in their daily practice. The previous findings from retrospective studies

show that early surgical treatment of these complications is advantageous. There is no profound evidence based algorithm on the access and surgical procedure up to date. However, transurethral and vaginal mesh excision techniques were demonstrated to be safe and successful in present studies. It is important to ensure a gentle tissue dissection and continuous follow-up after the surgery. The revision operations belong in the hands of experts and should be documented prospectively in trials and registries.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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Salvage Surgery after Failed Treatment of Synthetic Mesh Sling Complications

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Purpose: We report our experience with the diagnosis and treatment of refractory synthetic sling complications in women.

Materials and Methods: This is a retrospective study of consecutive women with failed treatments for mesh sling complications. Before and after surgery the patients completed validated questionnaires and voiding diaries, and underwent uroflow with post-void residuals, pad test, cystourethroscopy and video-urodynamic studies. Treatment was individualized, and results were subdivided into the 2 groups of conditions and symptoms. Outcomes were assessed with the Patient Global Impression of Improvement with success classified as a score of 1, improvement as 2 to 3 and failure as 4 to 7.

Results: A total of 47 women 35 to 83 years old (mean 60) had undergone at least 1 prior operation (range 1 to 4) to correct sling complications. Original sling composition was type 1 mesh in 36 patients and types 2 and 3 in 11. Surgical procedures included sling incision, sling excision, urethrolysis, urethral reconstruction, ureteroneocystotomy, cystectomy and urinary diversion, and enterocystoplasty. Median followup was 2 years (range 0.25 to 12, mean 3). Overall a successful outcome was achieved in 34 of 47 patients (72%) after the first salvage surgery. Reasons for failure were multiple for each patient. Of the 13 patients with treatment failure 9 subsequently underwent 14 operations. Success/improvement was achieved in 5 women (56%) after continent urinary diversion (1), continent urinary diversion and cystectomy (1), partial cystectomy and augmentation cystoplasty (1), biological sling and sinus tract excision (1), and vaginal mesh excision (1).

Conclusions: Success after the initial failure of mesh sling complications repair is possible but multiple surgeries may be required. Each symptom should be addressed separately.

Key Words: surgical mesh, suburethral slings, postoperative complications, salvage therapy, urinary incontinence

Abbreviations and Acronyms

LUTSS = Lower Urinary Tract Symptom Score
OAB = overactive bladder
PGI-I = Patient Global Impression of Improvement
Qmax = maximum flow rate
SUI = stress urinary incontinence
TOT = transobturator tape
TVT® = tension-free vaginal tape
UTI = urinary tract infection

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THE use of mesh for the correction of sphincteric incontinence has increased dramatically during the last 2 decades.[1,2] Its appeal rests in high reported success rates[3] and its comparatively simpler surgical technique which allows for greater numbers of surgeons to perform the surgery.[4] However, the initial enthusiasm for mesh has been tempered by increasing concerns about potential complications. In 2008 the Food and Drug Administration issued a public health warning about complications of synthetic mesh slings between 2005 and 2007.[5] By 2010 nearly 4,000

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reports of complications were submitted to the Food and Drug Administration (average 958 cases per year). The most frequent complications during this time were vaginal mesh erosion, pelvic pain, UTI, dyspareunia, organ perforation, voiding dysfunction and recurrence of incontinence.

The management of mesh sling complications is fraught with complexity and even in the most experienced hands the outcomes are suboptimal. We present our data on the presentation, surgical management and outcomes of salvage mesh repairs using validated outcome instruments at a tertiary care facility.

MATERIALS AND METHODS

This is a retrospective observational study of consecutive patients who presented with complications from synthetic mesh sling surgery and underwent at least 1 prior attempt at repair of the complication. Medical records from 1997 to 2012 were reviewed and patients were excluded from analysis if they did not undergo surgery and/or if they did not have at least 1 prior attempt at repair.

Baseline assessment at presentation included a 24-hour bladder diary, pad test (for incontinent patients), urinary flow rate, post-void residual volume, cystourethroscopy, videourodynamic studies and the validated LUTSS questionnaire. Treatment was individualized to particular complications. Postoperatively all patients completed a bladder diary, pad test (for incontinent patients), LUTSS questionnaire, uroflow and measurement of post-void residual volume, and the PGI-I for each preoperative symptom. Results were analyzed by presenting symptom and by anatomical condition (table 1). The primary outcome measure for symptoms was the PGI-I. A score of 1 correlated with success, a score of 2 to 3 indicated improvement and a score of 4 to 7 indicated failure. For anatomical conditions (urethral stricture, fistula, mesh erosion) the authors ascribed success, improvement or failure based on the specifics of each case.

Table 1. *Presenting symptoms and complications*

	No. (%)
Presenting symptoms:	
OAB	33 (70)
SUI	25 (55)
Recurrent UTI	10 (21)
Pelvic pain/dysuria	16 (34)
Obstructive symptoms	4 (9)
Vaginal discharge	8 (17)
Presenting conditions:	
Urethral obstruction	24 (51)
SUI	23 (49)
Bladder/urethral erosion	11 (23)
Fistula	8 (17)
Bladder/urethral stone	5 (11)
Vaginal extrusion	4 (9)
Ureteral injury	2 (4)

RESULTS

Overall 54 women were identified, of whom 5 were excluded from analysis because they had not undergone prior surgery for the mesh complication and 2 were excluded because they elected no further surgery. One patient was initially operated on at our institution and the remaining patients were referred from elsewhere. None of the original surgeries was performed by any of the authors. Mean patient age at presentation was 60 years (range 35 to 83). The time from mesh placement to the diagnosis of a complication was 1.99 years (range 1 month to 8 years). The mean number of attempts at repair before presentation was 1.3 (range 1 to 4). Type 1 (monofilament, macroporous) mesh was used in 36 patients (76.5%), and types 2 and 3 (multifilament, microporous) were used in 11 (23.5%). A retropubic approach was used in 41 (87%) women and a transobturator approach was used in 6 (13%). Table 1 lists the mesh complications by symptom and anatomical complication, and table 2 lists the types of salvage procedures performed.

Representative cases of sphincteric incontinence, urethral obstruction, urethral and bladder erosion, and vaginal extrusion are seen in figures 1 through 5, respectively. Followup ranged from 3 months to 12 years (mean 3 years, median 2 years). Time from salvage surgery to failure ranged from 4 months to 8 years with a mean of 2.2 years and a median of 2 years. Overall success/improvement was achieved in 34 of 47 (72%) patients after a single salvage operation. Reasons for failure were multiple for each patient, including refractory pain (9), mesh extrusion (8), OAB (8), mixed incontinence (2), urethral obstruction (1) and recurrent fistula (1). Of the 13 patients with initial treatment failure 9 subsequently underwent a total of 14 subsequent procedures, and success/improvement was achieved in 5 (56%) after continent urinary diversion (1); continent urinary diversion and cystectomy (1); partial cystectomy, ureteroneocystotomy and augmentation cystoplasty (1); biological sling and sinus tract excision (1); and vaginal mesh excision (1). Two patients underwent continent urinary diversion because of refractory low bladder compliance, detrusor overactivity and recurrent UTI after TVT. One patient underwent partial cystectomy,

Table 2. *Types of procedures performed*

	No.
Sling excision ± urethrolysis	16
Sling excision ± urethral reconstruction (including fistula repair) ± autologous fascial sling + Martius flap	14
Sling incision	10
Cystotomy ± partial cystectomy	5
Ureteroneocystotomy	2

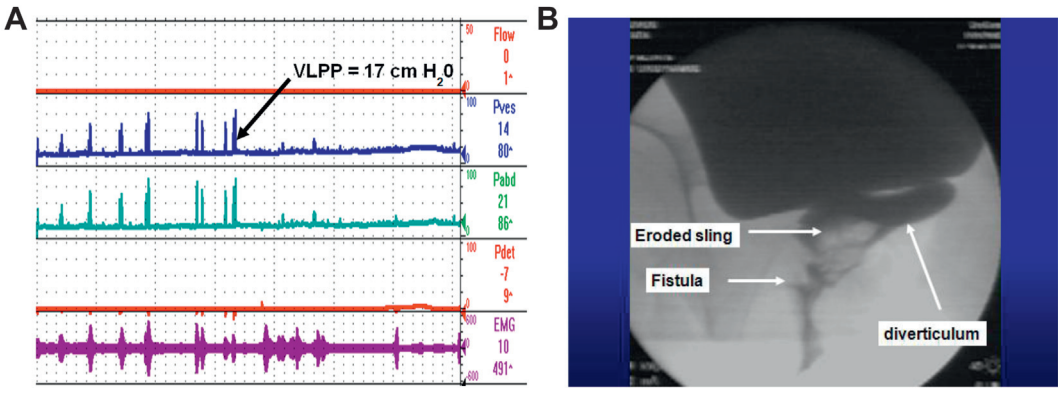

Figure 1. Videourodynamic study in 65-year-old woman who underwent urethral diverticulectomy and retropubic synthetic sling (type unknown). At cystoscopy large urethrovaginal fistula was visualized at bladder neck. *A*, urodynamic tracing showed vesical leak point pressure of 17 cm H_2O. *VLPP*, Valsalva leak point pressure. *Pves*, vesical pressure. *Pabd*, abdominal pressure. *Pdet*, detrusor pressure. *EMG*, electromyogram. *B*, stress cystogram showed sphincteric incontinence, large urethral diverticulum and urethrovaginal fistula. Patient underwent sling excision, urethrovaginal fistula repair with Martius flap interposition and autologous fascial pubovaginal sling. At postoperative year 6 PGI-I was 1 and patient denied having any lower urinary tract symptoms.

ureteroneocystotomy and augmentation cystoplasty because of mesh erosion of the sling into the bladder with resulting granuloma involving the bladder wall and ureteral obstruction. Per the patient specific PGI-I scores, success was ultimately achieved in 39 of 47 patients (82%) (table 3).

DISCUSSION

Synthetic mesh slings have become the most common operation for the treatment of sphincteric incontinence in women.[1] More than 1 million TVT procedures were performed between 1996 and 2007.[2] Despite a reported success rate of 84% for TOT slings and 88% for TVT slings in the most recent Cochrane review,[6] complications are significant and likely underreported. Studies suggest substantially higher complication rates than what has been reported in the peer reviewed literature.[2,7]

Only 1 patient in this series was operated on at our institution and there is no institutional database, so it was not possible for us to determine the incidence of mesh sling complications, and we acknowledge that our highly select series may overstate the incidence of mesh sling complications by implication. Nevertheless, we do believe that there is a small cohort of patients whose lives have been unalterably changed for the worse as a complication of these seemingly trivial and easy to perform operations. Given the increasing number of mesh sling operations performed and the complexity

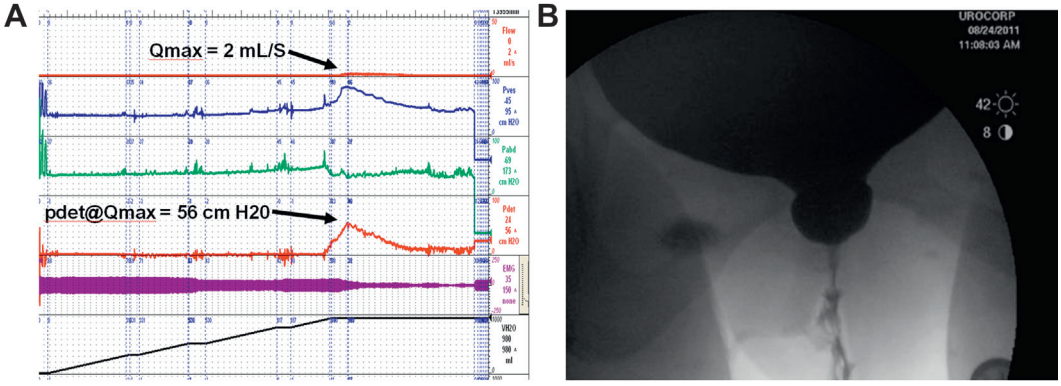

Figure 2. Urethral obstruction 2 years after SPARC™ sling. At surgery sling was embedded in urethral wall but did not erode. *A*, urodynamic tracing showed severe urethral obstruction, Blaivas-Groutz nomogram type 2. *pdet@Qmax*, detrusor pressure at maximum flow rate. *Pves*, vesical pressure. *Pabd*, abdominal pressure. *Pdet*, detrusor pressure. *EMG*, electromyogram. *VH_2O*, volume of water. *B*, x-ray at Qmax showed obstruction in distal third of urethra. Patient underwent excision of suburethral portion of sling and subsequently voided normally (Qmax 19 ml per second, voided volume 150 ml, post-void residual 49 ml). However, patient experienced sphincteric incontinence and underwent successful autologous fascial sling 4 months later.

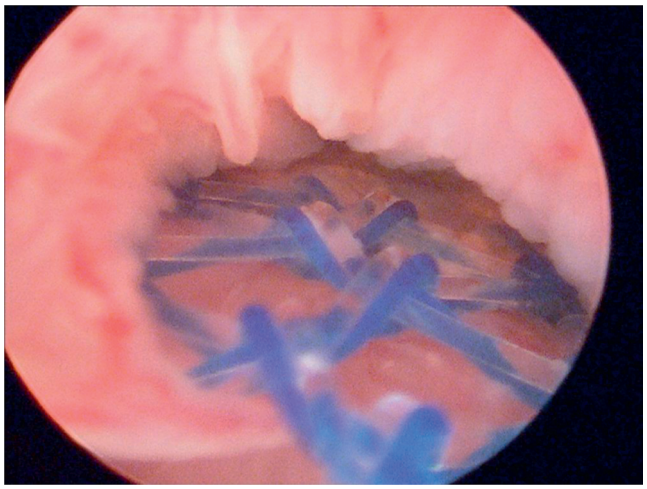

Figure 3. Urethral erosion of TVT in 48-year-old woman 1 year postoperatively. At surgery all tape was removed from affected site without need for reconstruction. At postoperative year 1 she reported PGI-I of 1.

of surgery to repair the complication(s), we believe that there will be an increasing number of patients in whom initial treatments failed and an increasing number of "mesh cripples." Our study is highly selective and is hardly representative of the typical

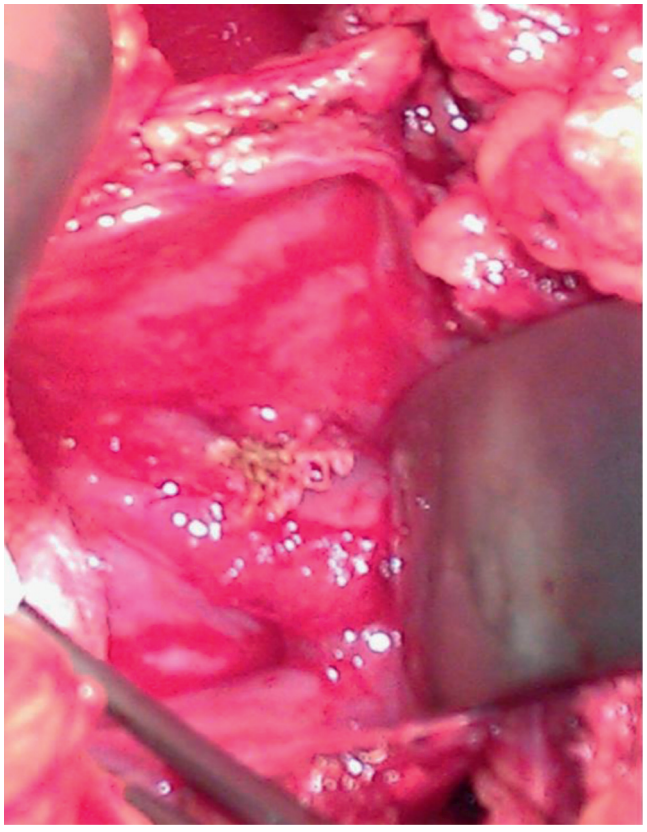

Figure 4. Bladder erosion 7 years after TVT

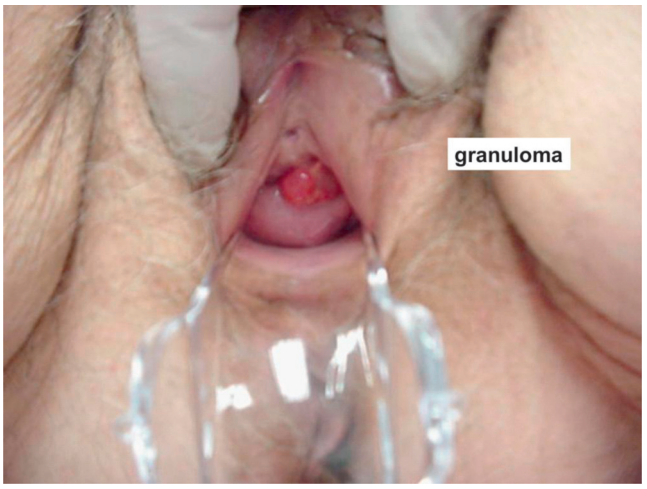

Figure 5. Vaginal extrusion of TOT sling with granuloma

case. However, it does shed some light on the severity and refractory nature of these problems.

The etiology of mesh sling complications is a matter of conjecture. Urethral obstruction and/or erosion have 3 potential causes, namely 1) the surgeon simply pulls the sling too tight at surgery, 2) a correctly placed sling contracts with time due to tissue ingrowth[8] and 3) faulty surgical technique results in placement of the sling directly into the urinary tract. Depending on the thickness of the vaginal wall, it may be difficult to place the mesh accurately. If it is placed too superficially (ie between the vaginal epithelium and the pubocervical fascia), vaginal extrusion might occur. Conversely, sling placement that is too deep (ie to the pubocervical fascia) might cause urethral or bladder erosion.

Regardless of the original cause, salvage treatment of urethral obstruction, erosion and/or fistula depends on intraoperative findings. In most patients it is possible to separate the remnant of

Table 3. *Outcomes by symptom complex and condition resolution*

	No. Success (%)	No. Improvement (%)	No. Failure (%)
Symptom (No.):			
OAB (35)	6 (17)	20 (57)	9 (26)
SUI (28)	11 (39)	12 (43)	5 (18)
Pelvic pain (18)	5 (28)	4 (22)	9 (50)
Discharge/hematuria (7)	4 (57)	2 (29)	1 (14)
Voiding dysfunction (4)	3 (75)	1 (25)	0 (0)
Condition (No.):			
Urethral obstruction (24)	16 (66)	6 (25)	2 (9)
Fistula (14)	13 (93)	0 (0)	1 (7)
SUI (25)	10 (40)	10 (40)	5 (20)
Vaginal extrusion (12)	4 (33)	0 (0)	8 (67)
Bladder/urethral erosion (11)	10 (91)	0 (0)	1 (9)
Ureteral injury (2)	2 (100)	0 (0)	0 (0)

the sling that was not previously excised from the urethra with sharp dissection and simply incise or excise the suburethral portion. If the sling is adherent to the wall or has eroded through the wall, we believe it best to excise as much of the sling as possible through the vagina and repair or reconstruct the urethra as necessary. If there is extensive periurethral scarring, urethrolysis may be necessary.

Determining the need for another sling and/or Martius flap must be individualized based on local anatomy and patient/surgeon preference. We strongly believe that when another sling is needed, it should be biological (we prefer autologous rectus fascia),[9] and have found that positioning the Martius flap between the reconstructed urethra and sling provides a good buffer against recurrence without compromising continence outcomes.[10] The American Urological Association Guideline on the treatment of SUI specifically warns against using another synthetic mesh sling once urethral erosion has occurred.[11] In the present study the success rates for treating urethral obstruction and fistula were high at 93% and 91%, respectively. Other studies have shown a 70% success rate for mesh slings[12] as well as an 87% success rate[13] and an 84% success rate for urethrolysis for obstruction after biological and mesh slings, respectively.[14]

For bladder erosions of the mesh (with or without stones) several approaches have been described. However, there are no meaningful data and no realistic method of comparing the results. Most commonly, surgeons have described transurethral removal with a scissors and/or grasping forceps, laser lithotripsy and vaporization of the mesh, a combined percutaneous and transurethral approach as well as combined transvaginal and suprapubic approaches.[15–17]

Our experience with the transurethral and percutaneous approach is limited. We have noted that in many instances of bladder and urethral perforation, the mesh crosses the wall of the viscus obliquely so that if one removes just the portion that is visible in the bladder, recurrence may be inevitable in some patients. After a recurrence we advocate removing all of the mesh from the offending site (vaginal and suprapubic). It is generally straightforward to remove the retropubic and vaginal portions of the sling, but for retropubic slings the portion adjacent to the bladder neck is particularly challenging, and may require a combined retropubic and vaginal approach.

The cause of pelvic pain and dyspareunia has also not been well studied. If the vagina is scarred, narrowed and tender, with or without mesh extrusion, the cause of the dyspareunia may be obvious. However, when that is not the case, proposed causes of refractory pain are nerve entrapment, infection and foreign body granuloma.[18,19]

Pelvic pain and dyspareunia pose particularly difficult challenges, and despite our best efforts treatment was unsuccessful in half of the patients. We hypothesize that inadequate removal of the mesh may be a cause of persistent pain, and we have been particularly frustrated by our inability to address this in patients with TOT slings and in those who have undergone mesh prolapse repairs. Reynolds et al reported a 63% improvement in pain symptoms after an attempt at complete removal of the mesh from sling and prolapse surgeries.[20] The discrepancy could be attributed to the different techniques used for removal (traditional vs obturator foramen dissection) or to the small patient population in the study by Reynolds et al.

There are several weaknesses in our study. The primary outcome measure, the PGI-I, was administered with reference to patient symptoms before the salvage procedure and not compared to patient status before the original sling surgery. We believe that most patients who reported improvement after the salvage surgery were actually worse off than before the initial mesh sling surgery. In addition, the retrospective nature of the study could be considered a weakness. Also, none of the patients underwent the original sling operation at our practice so we are unable to assess the incidence, natural history and time course of these complications. The followup was too short and it is likely that some of our successes will ultimately be failures in the future.

Strengths of this review include the fairly large size of our series, the use of well-defined and validated outcome tools that assessed subjective and objective criteria, and reasonably good followup.

No outcome instruments have been specifically devised to assess treatment of mesh complications. Most studies have defined success postoperatively based on patient subjective complaints.[21–23] In this study we assessed each symptom and condition separately. For incontinence, the Simplified Urinary Incontinence Outcome Score was used as the primary outcome measure[24] and for OAB the overactive bladder symptom score was used.[25] Voiding dysfunction and obstructive symptoms were assessed with a flow and post-void residual as well as the LUTSS questionnaire. A patient reported outcome, the PGI-I, was used to evaluate pelvic pain and dyspareunia as well as to provide an overall subjective appraisal of the success/failure of treatment.[26]

Using these outcome instruments, overall success/improvement was achieved in 34 of 47 (72%) patients after a single salvage operation and in 82%

after multiple operations. For individual symptoms and conditions, the success/improvement rate ranged from 50% (for pain) to 100% (for urethral obstruction). Padmanabhan et al detailed vaginal excision with subjective cure in 75% and improvement in 21%.[23] For repair of lower urinary tract erosions 53% reported subjective cure and 35% indicated improvement. Other studies used incontinence quality of life questionnaires, eg the Urogenital Distress Inventory (UDI-6) and Incontinence Impact Questionnaire (IIQ-7), in conjunction with a stress test.[27]

CONCLUSIONS

The true incidence of refractory mesh sling complications is not known, but it is evident that they do occur, and may be severe and lifestyle altering. Most patients have multiple symptoms and conditions. Nevertheless, some degree of success is possible in most patients, and for some conditions such as urethral obstruction, fistula, bladder and urethral erosions a high success rate is possible. The most difficult problem to treat is pain, with only 28% of patients with pain considering the salvage operation a success.

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Safety considerations for synthetic sling surgery

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Abstract | Implantation of a synthetic midurethral sling (SMUS) is the most commonly performed anti-incontinence operation in women worldwide. The effectiveness of the SMUS is comparable to that of the historical gold standards—autologous fascial slings and the Burch colposuspension. Much controversy, however, has evolved regarding the safety of this type of sling. Overall, the quality of the studies with respect to assessing risks of SMUS-associated complications is currently poor. The most common risks in patients with SMUS include urethral obstruction requiring surgery (2.3% of patients with SMUS), vaginal, bladder and/or urethral erosion requiring surgery (1.8%) and refractory chronic pain (4.1%); these data likely represent the minimum risks. In addition, the failure rate of SMUS implantation surgery is probably at least 5% in patients with stress urinary incontinence (SUI). Furthermore, at least one-third of patients undergoing sling excision surgery develop recurrent SUI. Considering the additional risks of refractory overactive bladder, fistulas and bowel perforations, among others, the overall risk of a negative outcome after SMUS implantation surgery is ≥15%.

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Introduction

The Burch colposuspension and autologous fascial pubovaginal sling have been considered the gold standard treatments of stress (sphincteric) incontinence (SUI), in women since the late 1990s.[1] Historically, pubovaginal slings had been reserved for women with complicated, severe and/or recurrent sphincteric incontinence,[2] but since the late 1990s these have been advocated for treatment of women with all types of sphincteric incontinence—simple and complicated.[3,4] Over the past decade, fueled by a stampede of innovations in synthetic sling composition, structure and implantation techniques and a surge in commercial marketing, implantation of the synthetic midurethral sling (SMUS) has emerged as the most frequently performed operation in women with SUI. Some authors suggest that, to date, over 3 million SMUS implantation procedures have been conducted worldwide, and more than 80% of these happened in the USA.[5] We have been unable to independently verify the number of SMUS implanted worldwide. But, by extrapolating the data from a population-based cohort study,[6] we estimate that approximately 500,000 SMUS were implanted in the USA between years 2001–2010 and that in the ensuing 4 years at least another 300,000 of these procedures were done. Considering the size of the population of the rest of the world and the fact that slings have been implanted *en masse* in most economically developed countries since at least the mid-1990s, a figure of 3 million procedures seems reasonable.[6] Furthermore, in an analysis of 7,200 case logs submitted by American urologists for their certifying credentials in 2013, 83% of operations performed for incontinence in women were SMUS implantations.[7]

SMUS implantation is an operation for the correction of sphincteric incontinence in which a synthetic plastic like mesh strip (the sling) is passed around the urethra into the retropubic space or beneath the urethra through the obturator foramen using trocars. Theoretically, when abdominal pressure rises, as in a cough or sneeze, the urethra is compressed by the sling, and the flow of urine is prevented, much like kinking of a garden hose. The appeal of such procedures is obvious—in theory. SMUS implantation is a minimally invasive, easy-to-perform procedure that is usually completed in under half an hour and, compared to traditional native tissue repairs, enables a much faster recovery with less perioperative morbidity than either the Burch colposuspension or autologous fascial slings. The effectiveness of this approach remains unchallenged. Numerous trials have shown SMUS to be as effective as the autologous fascial sling and Burch colposuspension, with moderate and/or high quality of evidence.[8]

Theory and practice often diverge, though, and this seems to be the case with SMUS. As more SMUS implantations are being performed and the longevity expectations of patients with SMUS are increasing, it has become apparent that unanticipated, serious, sometimes lifestyle-altering complications can occur that are not only unique to patients with SMUS but are also often refractory to treatment.[9,10] The purpose of this Review is to summarize the published literature regarding complications that are uniquely associated with SMUS and to present an overview of complications that are not unique to these slings.

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Competing interests
J.G.B. and V.I. have provided opinions as medicolegal expert witnesses in mesh litigation cases. J.G.B. has acted as a consultant for Astellas Pharma, is a shareholder in P Square Medical, and is a shareholder and co-owns intellectual property with LLC and Symptelligence Medical Informatics. The other authors declare no competing interests.

Key points

- The effectiveness of synthetic midurethral slings (SMUS) is comparable to the time-honoured gold standards—the autologous fascial sling and Burch colposuspension
- At least 15% of women with SMUS experience a serious adverse outcome and/or recurrent sphincteric incontinence
- A subset of women sustain refractory, lifestyle-altering complications that are unique to women with a SMUS
- SMUS-associated complications are under-reported
- The overall quality of the published evidence is currently low with respect to assessing SMUS safety and SMUS-associated complications

Transvaginal mesh slings

The retropubic tension-free transvaginal mesh tape (RP) sling procedure was introduced for treatment of SUI in 1995,[11] and was soon followed in 2001 by the transobturator tape (TOT) sling procedure, in which the sling is introduced via the obturator fossa instead of the retropubic space in an attempt to minimize the complications associated with use of RP slings.[12] Since the introduction of these procedures, results of many modifications of the RP and TOT sling procedures have been published, generally with a follow-up duration of <4 years; most studies had a follow-up duration of ≤1 year.

In a review of prospective randomized controlled trials investigating performance of RP and/or TOT slings, authors reported objective cure rates of patients treated with RP slings ranging between 83.9% and 100%, and 84% and 97.6% for those with TOT slings. Subjective cure rates for patients with RP or TOT slings were 64.5–94% and 60–92.9%, respectively. Median or mean follow-up duration of these studies ranged between 9 months and 24 months.[13] Thus, no notable differences in effectiveness have been revealed by meta-analyses of trials comparing the effectiveness of RP slings with that of TOT slings.[14,15]

More than 19 years have elapsed since the introduction of RP slings and 13 years for TOT slings; results regarding the long-term effectiveness of these treatments are, therefore, now available, with the longest series reporting a follow-up duration of 17 years.[16] Findings of over 200 studies of varying design and quality, investigating the effectiveness of either RP or TOT slings have been published. Of these, only six contain information on outcomes of patients followed up for >5 years and five have reported outcomes after a follow-up duration of 5 years (Table 1). Effectiveness of the treatments tested in these studies has been measured using a variety of subjective and/or objective outcome instruments. Subjective outcomes have been measured using detailed validated questionnaires such as the short urogenital distress inventory (SUDI), short incontinence impact questionnaire, the European quality of life questionnaire,[17] the patient global impression of improvement (PGII) questionnaire,[16,18] the visual/verbal analogue scale (VAS),[16,19–21] non-validated questionnaires[20,22] and telephone surveys.[23] In our judgement, however, the use of some of the validated outcome instruments does not provide sufficiently explicit data to be considered scientifically rigorous. For example, the urogenital distress inventory (UDI)-6 conflates bother with incontinence. This inventory contains the question "Do you experience and how much are you bothered by … leakage,"[24] from stress incontinence? This means a woman could leak only a few drops once a year and have a lot of bother or be totally incontinent and have no bother, yet record exactly the same score. Furthermore, variability in the use of validated and nonvalidated questionnaires might be another explanation of the discrepancies in reported outcomes and can complicate direct comparisons of results from different studies.

A variety of objective outcome instruments have also been used to measure outcomes of these long-term (follow-up duration ≥5 years) studies. The Valsalva stress test, in which the patient is asked to perform a Valsalva manoeuvre to increase abdominal pressure, or the cough test with a full bladder to provocatively test for the development of SUI are the most commonly used objective outcome measures.[17,18,20,21] However, these tests are not standardized and, typically, abdominal and vesical leak point pressures are not measured.[25] Other studies involved checking bladder volume by ultrasonography or just verbally confirming that the patient feels that their bladder is "comfortably full"[26] or "full"[18,27] and then asking the patient to cough. One group asked the patient to do "20 jumping jacks and 3 forceful coughs"[22] or "10 coughs in the standing position"[22] with a 300 ml bladder volume to check for SUI.[22]

The pad-weight test is another objective measurement used to assess treatment outcomes. A variety of pad-weight tests were used in these long-term studies including a 1-hour pad-weight test,[19] a 24-hour pad-weight test[28] and a 48-hour pad-weight test[29] with a result of ≤1 g increase in pad weight defining cure. Two studies used urodynamic evidence of the absence of leak on performing a Valsalva manoeuvre to indicate postoperative success either as a primary endpoint or as an adjunctive measure.[17,18]

Of published series with follow-up durations ≥5 years, the largest consisted of 707 patients and the smallest consisted of 55 patients.[16–23,26,27,29] Overall, objective cure rates of patients with SUI after treatment with either TOT or RP slings at or after a follow-up duration of 5 years ranged between 71% and 92%, and subjective cure rates between 65% and 90.3%. By combining subjective measures of cure and improvement, treatment effectiveness increased from 76% to 95% (Table 1).[16–23,26,27,29]

The series with the longest reported follow-up duration (17 years) was a prospective, single-institution study of 90 women who underwent the (original) RP sling implantation procedures at Uppsala University.[16] The overall rate of subjective cure or improvement assessed using the PGII score was 87% and the objective cure rate assessed using a cough stress test was 91%. Between follow-up years 5 and 17, objective cure rates declined very little—from 94% to 91%—and subjective cure or improvement decreased from 95% to 87%. However, 11 of 53 evaluable patients said that they

Table 1 | Long-term (follow-up duration >5 years) studies of SMUS effectiveness

Study characteristics	Patient characteristics	Mean follow-up duration (months)	Outcome Instrument	Outcomes*
Prospective studies				
Angioli *et al.* (2010)[20] *n* = 72	Outcomes of 69 patients with RP or TOT slings were evaluated; 4.1% were lost to follow up	60	ST, NVQ,‡ VAS‡	Objective cure reported in 71% and 73% in patients with RP or TOT slings, respectively; Subjective cure reported by 60% and 62% of patients with RP or TOT slings, respectively
Groutz *et al.* (2011)[23] *n* = 60	Outcomes of 52 patients with RP slings were evaluated; 13.3% were lost to follow up	60	NVQ‡	Subjective cure reported by 65% of patients
Groutz *et al.* (2011)[27] *n* = 65	Outcomes of 61 patients with TOT slings were evaluated; 6.1% were lost to follow up	60	ST, NVQ‡	Objective cure reported in 74% of patients, 8% had improved symptoms and 18% subjectively reported treatment failure
Cheng *et al.* (2012)[17] *n* = 103	Outcomes of 100 patients with TOT slings were evaluated; 2.9% were lost to follow up	65	VUD, QOL,‡ VAS‡	Objective cure reported in 87.4% of patients; subjective cure reported by 78% of patients
Nilsson *et al.* (2013)[16] *n* = 90	Outcomes of 58 patients with RP slings were evaluated; 23.3% were lost to follow up	201	ST, VQ‡	Objective cure reported in 91.3% of patients; subjective cure reported by 87%
Serati *et al.* (2013)[18] *n* = 191	Outcomes of 185 patients with TOT slings were evaluated; 3.1% were lost to follow up	60	ST, VQ‡	Objective cure reported in 90.3% of patients; subjective cure reported by 90.8%
Svenningsen *et al.* (2013)[22] *n* = 603	Outcomes of 483 patients with RP slings were evaluated; 19.9% were lost to follow up	120	Exercise + PT, VQ,‡ NVQ‡	Objective cure reported in 89.9% of patients; subjective cure reported in 76.1% of patients; 18% had improved symptoms; 5.9% had treatment failure
Retrospective studies				
Ankardal *et al.* (2006)[29] *n* = 707	Outcomes of 271 patients with RP slings were evaluated; 5.0% were lost to follow up	60§	ST, 48 h PT (NVQ,‡ VAS‡)	Objective cure reported in 83% of patients; subjective cure reported by 73.1% of patients; 15.9% had improved symptoms; 11% had treatment failure
Olsson *et al.* (2010)[21] *n* = 147	Outcomes of 104 patients with RP slings were evaluated; 15.6% were lost to follow up	138	ST	Objective cure reported in 84% of patients; subjective cure reported by 77% of patients; 18% had improved symptoms; 5% had treatment failure
Li *et al.* (2012)[19] *n* = 55	Outcomes of patients with RP slings were evaluated; percentage of patients lost to follow up not reported	81.85	1 h PT (NVQ‡)	Objective cure reported in 85.5% of patients; subjective cure reported in 74.6% of patients; 7% had improved symptoms; 25.6% had treatment failure
Athanasiou *et al.* (2014)[26] *n* = 145	Outcomes of 124 patients with TOT slings were evaluated; 14.4% were lost to follow up	90.3	ST (VQ‡)	Objective cure reported in 81.5% of patients; subjective cure reported in 83.1% of patients; 3.2% had improved symptoms; 13.7% had treatment failure

*Owing to a lack of uniformity in reporting efficacy (improved and failed), improvement and failure were assumed to be based on subjective responses. Incidence of failure was calculated by subtracting the sum of subjective cured and improved responses from 100%. Improved patients were mutually exclusive to cured patients reported. ‡Indicates a subjective outcome instrument. §Indicates actual, not mean follow-up duration. Abbreviations: NVQ, nonvalidated questionnaire; PT, pad-weight test; QOL, quality of life; RP, retropubic tension-free transvaginal mesh tape; SMUS, synthetic midurethral slings; ST, cough or valsalva stress test; TOT, transobturator tape; VAS, visual analogue scale; VQ, validated questionnaire; VUD, videourodynamics.

"experienced leakage during straining".[16] The authors attributed this symptom to the development of severe urge incontinence, which might or might not have been caused by the RP sling itself. However, this study was hindered by the fact that 32 of 90 patients (36%) were not included in the analysis after a follow-up duration of 17 years as 11 (12%) women died, five (6%) had mental impairment and 16 (18%) were lost to follow-up. Overall, 58 (64%) women were available to have their 17-year outcomes evaluated, of whom 46 (51%) women were evaluated in the clinic and 12 (13%) were interviewed by telephone.

By contrast, in another investigation,[30] researchers using much more stringent outcome criteria found the 2-year objective success rate of RP and TOT slings was 77% and 72.3%, respectively and the subjective success rates were 56% and 48%—nearly a 40% reduction in subjective success compared with results from the Uppsala cohort.[16] In this randomized study of 597 patients, objective success was defined as a negative provocative stress test, a negative 24-hour pad-weight test and no need for retreatment of SUI.[27] Subjective success was defined as the absence of self-reported symptoms of SUI on the Medical, Epidemiological and Social Aspects of Aging questionnaire and no urine leakage recorded in a 3-day voiding diary.

The overall effectiveness of RP or TOT slings reported in these long-term studies of patients with SUI has been generally high, although some of the reported success occurred after a secondary operative procedure or medical intervention.[17,19,21,26] Thus, for patients who developed mesh erosion and had successful revision surgery, studies would typically report this as a successful outcome. Secondary treatments for those who develop *de novo* urge incontinence have not been reported, although if the RP or TOT sling procedures are effective in these patients they would typically be included in the 'subjectively cured' or 'improved' category.

The percentage of patients who were lost to follow up should also be carefully noted. In patients who were lost to follow up because of death, the cause of death and

Table 2 | Complications of either RP or TOT slings

Complication	*n*	Complications (% of patients)	Incidence (mean; range)
General complications			
Death within 30 days*	7,762	0 (0.0)	0.0
Urethral obstruction/voiding dysfunction	25,586	1,403 (5.5)	7.3; 0–33.9
Urethral obstruction requiring surgery	9,375	301 (3.2)	2.3; 0–21.3
Urinary infections	13,296	598 (4.5)	7.3; 0–39.1
Pain (within 6 weeks)	5,097	374 (7.3)	7.9; 0–33.3
Neurologic symptoms (within 6 weeks)	1,769	42 (2.4)	1.2; 0–10.3
De novo OAB	14,765	1,512 (10.2)	10.9; 0–48.1
Pelvic organ perforation			
In total	20,630	681 (3.3)	3.5; 0–16.1
Bladder	19,411	579 (3.0)	2.9; 0–16.1
Vaginal	5,521	91 (1.6)	1.4; 0–14.1
Urethral	4,541	6 (0.1)	0.0; 0–1.5
Bowel	3,820	4 (0.1)	0.0; 0–1.7
Ureteral	3,820	1 (0.0)	0.0; 0–1.3
Mesh exposure/erosion/extrusion			
In total	17,520	475 (2.7)	2.5; 0–26.1
Treated conservatively	15,403	112 (0.7)	0.9; 0–7.1
Vaginal	13,496	78 (0.6)	0.7; 0–7.1
Bladder	13,496	5 (0.0)	0.0; 0–5.6
Urethral	13,496	0 (0.0)	0.0
Requiring surgery	16,619	333 (2.0)	1.8; 0–26.1
Vaginal	13,705	235 (1.7)	1.5; 0–15.9
Bladder	13,393	29 (0.2)‡	0.2; 0–15.2
Urethral	13,628	11 (0.1)	0.2; 0–16.7
Longer-term complications			
Refractory pain (>6 weeks)	7,084	247 (3.5)	4.1; 0–30.5
Neurologic symptoms (>6 weeks)	2,449	51 (2.0)	1.0; 0–10.6
Fistulas	710	2 (0.3)	0.3; 0–1.1

*No deaths were reported in peer-reviewed publications, although 7 were reported in the MAUDE database. ‡Three studies removed from incidence calculation because these were case series of just bladder erosions. Abbreviations: MAUDE, manufacturer and user facility device experience; OAB, overactive bladder; RP, retropubic tension-free transvaginal mesh tape; TOT, transobturator tape.

whether it might have been related to having a TOT or RP sling has not been reported. In addition, long-term studies often featured a lack of follow up in a substantial number of patients. In these long-term studies, between 5% and 36% of patients were either deceased or unavailable for follow up for other reasons (Table 1).

In summary, the long-term effectiveness of RP or TOT slings, as measured by subjective and/or objective instruments suggests that rates of cure or improvement of SUI after implantation are high and compare favourably to the traditional gold standard—the autologous pubovaginal sling. These results might, however, be overly optimistic owing to a host of factors including the suboptimal outcome instruments used, inclusion of patients who might have required multiple procedures and the loss of a substantial number of patients to follow-up monitoring.

SMUS complications

Mesh sling complications can be caused by a host of factors: intraoperative transgressions (such as viscus or vaginal perforation and nerve injury);[31] bacterial contamination;[32] improper tensioning of the sling—either too tight or too loose; host–foreign-body reaction;[33] tissue ingrowth;[34,35] and changes that the mesh undergoes once implanted, such as degradation, curling, banding and leaching of substances into the surrounding tissues (Tables 2–5).[36–38]

Evaluating the incidence, severity and consequences of the various RP and/or TOT sling complications is a daunting task. Of the thousands of published studies, only a few were even designed to track complications in any meaningful way. The short follow-up duration of most of these studies and the lack of accounting for those lost to follow up are additional confounders. In addition, complications might arise that were not even recognized when the original studies were conducted, such as banding as a cause of dyspareunia, which was first described in 2010.[38] Furthermore, all studies are hampered by an absence of the patient's own perception of the severity of the complication. For example, one study[39] that included pain lasting >6 weeks as a category of complication was published, but there is no mention of the severity of this pain, effect on quality of life nor how long the pain actually lasted. For some patients, this pain is treatment-refractory and lifestyle-altering, yet no metric exists that describes this category of complication in sufficient detail. The effects of long-term pain receive no attention at all in any study except for a few case studies of complications.[9,40–44]

The concomitant, widespread use of two different generic sling designs (RP and TOT) with different implantation techniques and at least 41 different commercially available kits,[42] each having different sling and trocar characteristics with potentially different complication profiles, confounds accurate analysis of sling complications. These different characteristics might also portend different complication profiles, yet studies of sling complications almost never distinguish between the different kit types and many do not even separate TOT from RP slings.

Considerable evidence exists that SMUS complications are underreported. Discrepancies exist between the SMUS complication rates reported by urologists from individual institutions, those reported in the literature, the (unreported) experience of tertiary care practices and those in the MAUDE (Manufacturer and User Facility Device Experience) database.[10,40,45] For example, in a population-based cohort of 45 million commercially insured individuals in the USA, investigators found the cumulative risk of requiring sling removal owing to voiding dysfunction or mesh extrusion and/or erosion to be 3.7% (95% CI 3.5–3.9%) after a follow-up duration of 9 years.[6] Furthermore, this study[6] excluded patients whose slings were removed owing to pain and other indications, thus the actual incidence of sling removal owing to complications is probably even higher than that. Extrapolating from this estimate and the estimated number of slings implanted in the

Table 3 | Complications of RP slings

Complication	*n*	Complications (% of patients)	Incidence (mean; range)
General complications			
Death within 30 days	3,499	0 (0.0)	0.0
Urethral obstruction/voiding dysfunction	16,301	704 (2.8)	8.8; 0–32.7
Requiring surgery	6,875	223 (2.4)	2.7; 0–8.9
Urinary infections	8,936	327 (3.7)	8.6; 0–39.1
Pain (within 6 weeks)	2,133	111 (5.2)	4.5; 0–23.1
Neurologic symptoms (within 6 weeks)	520	14 (2.7)	1.6; 0–5.0
De novo OAB	7,989	925 (11.6)	11.4; 0–29.4
Pelvic organ perforation			
In total	13,164	498 (3.8)	4.8; 0–14.3
Bladder	12,929	480 (3.7)	4.6; 0–14.3
Vaginal	763	11 (1.4)	1.0; 0–2.1
Urethral	1,224	4 (0.3)	0.0; 0–1.5
Bowel	800	4 (0.5)	0.0; 0–1.7
Ureteral	800	0 (0.0)	0.0
Mesh exposure/erosion/extrusion			
In total	8,303	179 (2.2)	2.3; 0–26.1
Treated conservatively	7,168	44 (0.6)	0.1; 0–5.6
Vaginal	6,193	22 (0.4)	0.0; 0–4.6
Bladder	6,193	5 (0.1)	0.0; 0–5.6
Urethral	6,193	0 (0.0)	0.0
Requiring surgery	7,902	135 (1.7)	1.6; 0–26.1
Vaginal	6,621	79 (1.2)	1.0; 0–10.9
Bladder	6,386	26 (0.4)	1.4; 0–15.2
Urethral	6,621	4 (0.1)	0.3; 0–16.7
Longer-term complications			
Refractory pain (>6 weeks)	2,328	42 (1.8)	2.0; 0–7.9
Neurologic symptoms (>6 weeks)	908	19 (2.1)	1.0; 0–5.2
Fistulas	388	1 (0.2)	0.4; 0–0.7

Abbreviations: OAB, overactive bladder; RP, retropubic tension-free transvaginal mesh tape.

USA (80% of 3 million slings worldwide),[5] approximately 88,000 removal procedures should have occurred, yet we could find only 740 such procedures that have been reported in peer-reviewed publications.[17,18,20,26,31,43,46–99] An additional 7,654 mesh removals are reported in patient series investigating sling complications.[6,9,10,41,44,100–114] Use of imperfect research methodologies, a lack of long-term follow up and reporting bias have been suggested as causes of these differences.[10,45,115,116]

Safety and risk:benefit considerations

Safety of SMUS surgery refers to the probability of any adverse event, while risk describes the range and probability of specific adverse events. Demonstrating risk is relatively easy, but assessing safety is much more difficult. Any known adverse event is a risk, regardless of how infrequently the event has been reported or observed. Even a single case report of an adverse event establishes the existence of a specific risk, although without knowing the denominator, accurate assessments of the safety of sling surgery are impossible. The problem, simply stated, is that no well-controlled long-term safety studies with published results currently exist, nor do any good registries in this area. In lieu of this lack of conclusive evidence, we present current data, which, at its best, represent the minimum risks associated with SMUS implantation and long-term use (Tables 1 and 2). Major risks of SMUS surgery, which should be weighed up by patients considering undergoing these procedures, include those requiring further surgery and those that are refractory to treatment. Complications that lead to further surgery include urethral obstruction (3.2%), vaginal, bladder and/or urethral erosion (2%) and fistulas (0.3%). In addition, we estimate that bowel perforation and serious infections have a combined incidence of about 0.1%.[117–134] Refractory and potentially lifestyle-altering complications include chronic pain (4.1%) and *de novo* overactive bladder (OAB) in 11% (Table 5), although the number of patients with *de novo* OAB who are refractory to treatment remains unknown. Evidence suggests that well over 50% of patients with OAB of any aetiology discontinue medical treatment within 1 year, owing to a combination of poor effectiveness and low tolerability.[135–137] For the purposes of this discussion we made a conservative estimate that 35% of patients with *de novo* OAB following SMUS surgery are refractory to treatment, which suggests that approximately 3.9% of patients who have undergone SMUS surgery will have refractory OAB (Box 1).

Establishing safety, defined as the chances of having an unsatisfactory outcome following sling surgery, is an important step in enabling accurate patient decision making. Many patients with both chronic pain and *de novo* OAB have previously undergone SMUS revision surgery; however, simply adding together the complication incidences to give an accurate indication of safety is impossible, as the available data are not sufficiently reliable to produce an accurate estimate this way. For the purposes of this discussion, we have made our best estimate of the safety of SMUS surgery utilizing the data summarized in the preceding paragraph.

The reported 5-year failure rate of SMUS surgery in patients with SUI ranges from 5% to 26% (Table 1),[16–23,26,27,29] and the reported incidence of *de novo* SUI after sling excision surgery ranges from 10–62%.[9,43,78,84,85,94,100,138] From these data, we estimate the lowest rate of recurrent and/or persistent SUI among patients who underwent SMUS surgery to be 5.3%. Furthermore, we conclude that the lowest estimated risk of serious complications of SMUS surgery is 13.6% and the additional risk of failure with respect to the original procedure (with respect to SUI) is 5.3%. These estimated data reflect the minimum risks reported in the literature, the actual risks could be considerably higher.

The ability of both physicians and patients to make informed decisions regarding sling surgery is predicated on an accurate understanding of the risk:benefit ratio. The benefits of sling surgery, with respect to effectiveness, have been well documented. By contrast, the risks associated with SMUS surgery are poorly understood

Table 4 | Complications of patients with a TOT sling

Complication	*n*	Complications (% of patients)	Incidence (mean; range)
General complications			
Death within 30 days*	4,044	0 (0.0)	0.0
Urethral obstruction/voiding dysfunction	8,287	406 (4.9)	5.9; 0–33.9
Requiring surgery	5,001	75 (1.5)	2.0; 0–21.3
Urinary infections	4,003	226 (5.6)	6.2; 0–23.3
Pain (within 6 weeks)	2,964	262 (8.8)	10.2; 0–33.3
Neurologic symptoms (within 6 weeks)	1,249	28 (2.2)	0.9; 0–10.3
De novo OAB	6,215	519 (8.4)	10.3; 0–48.1
Pelvic organ perforation			
In total	5,856	143 (2.4)	2.3; 0–16.1
Bladder	4,872	60 (1.2)	1.1; 0–16.1
Vaginal	4,582	80 (1.7)	1.6; 0–14.1
Urethral	4,296	2 (0.0)	0.0; 0–0.3
Bowel	3,020	0 (0.0)	0.0
Ureteral	3,020	1 (0.0)	0.0; 0–1.3
Mesh exposure/erosion/extrusion			
In total	8,293	196 (2.4)	2.7; 0–19.0
Treated conservatively	7,648	64 (0.8)	1.0; 0–7.1
Vaginal	6,739	52 (0.8)	1.0; 0–7.1
Bladder	6,739	0 (0.0)	0.0
Urethral	6,739	0 (0.0)	0.0
Requiring surgery	7,901	132 (1.7)	1.9; 0–15.9
Vaginal	6,528	98 (1.5)	1.8; 0–15.9
Bladder	6,528	3 (0.0)*	0.0
Urethral	6,528	7 (0.1)	0.0; 0–2.6
Longer-term complications			
Refractory pain (>6 weeks)	4,756	204 (4.3)	5.3; 0–30.5
Neurologic symptoms (>6 weeks)	1,541	32 (2.1)	0.9; 0–10.6
Fistulas	322	1 (0.3)	0.2; 0–1.1

*Case series only investigating bladder erosions were removed from the analysis. Abbreviations: OAB, overactive bladder; TOT, transobturator tape.

and poorly documented. Some risk factors, such as prior pelvic radiation or surgery, concomitant urethral diverticular surgery, the surgical learning curve and an individual surgeon's skill set are accepted risk factors, yet even these risk factors are not well documented in peer-reviewed publications. Thus, accurately prognosticating the risks of SMUS surgery for any particular patient is difficult.

Owing to the limitations inherent in the evaluation of risk and safety described in this section, we can estimate that, based on the available literature reports, a minimum of 12.5% of women who undergo mesh SMUS surgery have a serious adverse event and/or surgical failure, although limited data are available on prognostic indicators.

Perioperative complications

Methods used to identify and classify perioperative complications vary widely between studies. A classification system originally devised in 2004 based on severity of complications[139] was modified for use by the Urinary Incontinence Treatment Network, a multicentre collaboration supported by the National Institute of Diabetes and Digestive and Kidney Diseases, a branch of the NIH.[30,39,140,141] Investigators in this network defined minor complications (or minor adverse events) as those not requiring surgical intervention that were treated expectantly or with medication (grade 1–2). Major complications (serious adverse events) include those requiring one or more surgical procedures, and life-threatening complications are defined as those requiring management in an intensive care unit and often resulting in patient death (grade 3–5).[30] Bladder or urethral trocar perforation was considered to be a serious adverse event whether or not further intervention was necessary. Another classification scheme, the Accordion system,[120] enables postoperative complications to be categorized into in four levels of severity: mild, moderate, severe, and death.[44,142]

However, sorting complications into groups based solely on the severity of their presentation and treatment might be misleading in the absence of adequate follow-up monitoring. For example, patients with apparently minor complications such as vaginal exposure that is initially treated with local excision and primary closure might present with dyspareunia or recurrent exposure long after the follow-up period has expired.[9,31,41–44] Indeed, many patients in one of our own studies presented in exactly this way, but this fact was never captured in the paper owing to the methodology used.[9] We have seen many unreported examples of patients managed conservatively with short-term success, who ultimately presented with a recurrent complication that occurred after the study ended, owing to the short follow-up duration of most published research (1–2 years) relative to the expected lifespan of most implanted slings.[9,81,105,143–147] Authors of one study estimated the overall incidence of vaginal extrusion of mesh and pelvic pain to be 6% and 4.3%, respectively.[45] Despite peer-reviewed literature in this area being replete with statements about the short-lived nature of sling-related complications, most case reports of mesh sling complications document the treatment-refractory nature and suboptimal outcomes associated with these complications, none of which was captured by the original studies.[9,43] For some complications (cystitis, voiding dysfunction, pain or neurological symptoms), most authors claim that only expectant or medical treatment is necessary and that patient outcomes are satisfactory, without presenting any meaningful follow-up data to substantiate these claims.[30,146,148,149]

In 2011, the International Urogynaecology Association (IUGA) and the International Continence Society (ICS) published a joint recommendation for a standardization of terminology to report complications related to the insertion of prostheses and grafts in female pelvic floor surgery.[150] To date, these guidelines have not been widely used. The net result of all of this is that the science of assessing and reporting midurethral sling complications is seriously flawed.

Table 5 | Comparison of complications of patients with an RP sling or TOT sling

Complication	RP sling (mean; range)	TOT sling (mean; range)	Combined RP and TOT sling (mean; range)
General complications			
Death within 30 days	0.0	0.0	0.0
Urethral obstruction/voiding dysfunction	8.8; 0–32.7	5.9; 0–33.9	7.3; 0–33.9
Requiring surgery	2.7; 0–8.9	2.0; 0–21.3	2.3; 0–21.3
Urinary infections	8.6; 0–39.1	6.2; 0–23.3	7.3; 0–39.1
Pain (within 6 weeks)	4.5; 0–23.1	10.2; 0–33.3	7.9; 0–33.3
Neurologic symptoms (within 6 weeks)	1.6; 0–5.0	0.9; 0–10.3	1.2; 0–10.3
De novo OAB	11.4; 0–29.4	10.3; 0–48.1	10.9; 0–48.1
Pelvic organ perforation			
In total	4.8; 0–14.3	2.3; 0–16.1	3.5; 0–16.1
Bladder	4.6; 0–14.3	1.1; 0–16.1	2.9; 0–16.1
Vaginal	1.0; 0–2.1	1.6; 0–14.1	1.4; 0–14.1
Urethral	0.0; 0–1.5	0.0; 0–0.3	0.0; 0–1.5
Bowel	0.0; 0–1.7	0.0	0.0; 0–1.7
Ureteral	0.0	0.0; 0–1.3	0.0; 0–1.3
Mesh exposure/erosion/extrusion			
In total	2.3; 0–26.1	2.7; 0–19.0	2.5; 0–26.1
Treated conservatively	0.1; 0–5.6	1.0; 0–7.1	0.9; 0–7.1
Vaginal	0.0; 0–4.6	1.0; 0–7.1	0.7; 0–7.1
Bladder	0.0; 0–5.6	0.0	0.0; 0–5.6
Urethral	0.0	0.0	0.0
Requiring surgery	1.6; 0–26.1	1.9; 0–15.9	1.8; 0–26.1
Vaginal	1.0; 0–10.9	1.8; 0–15.9	1.5; 0–15.9
Bladder	1.4; 0–15.2	0.0*	0.2; 0–15.2
Urethral	0.3; 0–16.7	0.0; 0–2.6	0.2; 0–16.7
Longer-term complications			
Refractory pain (>6 weeks)	2.0; 0–7.9	5.3; 0–30.5	4.1; 0–30.5
Neurological symptoms (>6 weeks)	1.0; 0–5.2	0.9; 0–10.6	1.0; 0–10.6
Fistulas	0.4; 0–0.7	0.2; 0–1.1	0.3; 0–1.1

*Case series only investigating bladder erosions were removed from the analysis. Abbreviations: OAB, overactive bladder; RP, retropubic tension-free transvaginal mesh tape; TOT, transobturator tape.

Infection

In a randomized study of SMUS effectiveness, investigators found culture-proven cystitis in 8.4% of patients with RP and 4.7% with TOT slings.[30] In another study, the authors reported that 12% of patients developed at least one UTI in the first 3 months after RP sling surgery.[151] Our literature search documented bacterial cystitis in 0–39% of patients who underwent SMUS surgery (REFS 13,18,21–23,30,39,47,48,50,53,55–57, 59,61,66,74,76,83,91,152–186). Unfortunately, limited published data are available on the long-term consequences of these infections. For example, in one study, 7.3% of women had recurrent UTIs 12 months after being fitted with a TOT sling, but no published reports of longer-term follow-up currently exist.[76]

Other more serious infections have been reported after SMUS implantation. In a comprehensive literature review[45] several such complications following sling placement were reported: cellulitis;[117–121,187] abscess formation, including in the retropubic space,[122] retroperitoneal space,[123] thigh,[123] obturator space[124–126] and ischiorectal fossa;[127,128] sinus tract formation;[129] necrotizing fasciitis;[130] osteitis pubis;[131] and sepsis.[12] Thigh abscesses, a complication unique to the TOT sling approach, have been reported in the past decade.[101,123,188,189] Occurrence of such serious SMUS-related infectious complications is often delayed by months or years after sling implantation. Presenting symptoms include chronic discharge from the vagina, thigh and/or perineum.

Treatment of infected mesh and abscesses requires open drainage and removal of all mesh, which, otherwise, will serve as a nidus for further infection. Amid types II and III mesh materials,[190] such as Silastic® (Dow Corning, MI, USA) and Gore-Tex® (W.L. Gore & Associates, DE, USA), are easily identified and pulled out, usually in their intact form. The technical challenges of removing type I meshes are considerably greater. For example, even though the entire mesh is likely to be infected, only part of it is involved in the abscess. This part is easy to remove, but because of tissue ingrowth and probable degradation, the remaining mesh is usually embedded in the tissue and might fragment during dissection. Furthermore, the retropubic and thigh portions of RP and TOT slings, respectively, are notoriously difficult to remove.[9,43,78,84,85,94,100,138] RP slings are often adherent to the bladder neck and difficult to access during surgery. We, and others, have noted that the infection can track along muscle planes and even form a psoas muscle abscess in some patients.[123,191] These abscesses might require multiple operations in order to achieve a satisfactory outcome. Unfortunately, owing to the technical reasons explained above and concerns about complications in adjacent organs during the dissection, complete mesh removal is often not accomplished in patients with type I mesh slings. Necrotizing fasciitis (Fournier gangrene) has also been reported after both RP[192] and TOT[193] sling implantations. In patients with SMUS-related infections, removal of the complete mesh is particularly important. Of course, many more serious infectious complications are likely to arise from the 'minor' ones listed above,[113,126] but we could find no published studies that actually address this issue.

Pelvic organ perforations

Pelvic organ (bladder, urethral, vaginal [REFS 10,14, 16,18,21–23,30,33,39,47,48,50,52,53,55,56,59,62–64, 66,67,69–71,73,74,76,77,80,81,86–88,90–93,98, 99,109,132–134,140,145,146,148,151–153,156,158, 162,163,167,168,171,173,176–179,181–184,194–238], or bowel) perforation at the time of trocar passage has been reported to occur in 0–16% of sling surgery procedures (0–14% for RP sling implantation and 0–16% for TOT sling implantation). In most reports, the authors usually downplay any substantial implications of pelvic organ perforations. Authors will typically state that

Box 1 | Summary of mesh safety

Complications requiring surgery

- Urethral obstruction 3.2%
- Erosion, extrusion or exposure 2.0%
- Fistulas 0.3%
- Bowel injury or infection 0.1%
- Lifestyle-altering complications
- Chronic pain 4.3% (0.5%)*
- Refractory (*de novo*) OAB 11% (3.9%)*
- Recurrent and/or persistent SUI 5.3%
- Total incidence of serious complications and/or sling failure in patients with incontinence 15.3%

*Indicates numbers are not mutually exclusive to individual complications. For example, a patient who underwent mesh excision for exposure may develop refractory pain. The numbers in parenthesis refer to the estimated incidence of complications refractory to medical or surgical treament. Abbreviations: OAB, overactive bladder; SUI, stress urinary incontinence.

recognized trocar perforations of the bladder might be treated by simply removing the trocar (or sling) and passing it again and, at the discretion of the surgeon, leaving an indwelling catheter in for a matter of days or, sometimes, not at all.[148,239–242] However, in an article published in 2014, the authors concluded that occurrence of bladder and/or urethral perforations during surgery is associated with an almost 26-fold increase in risk of subsequent bladder or urethral mesh erosion.[31] If the findings of this study are accurate, the dictum of simply removing and repassing the trocar after bladder perforation must be seriously questioned.

Limited information is available on urethral complications following perforation, but if a perforation large enough to necessitate repair exists, most would agree that it is best to abandon the SMUS procedure.[39,62,64,73,140,213] Depending on the circumstances, buttressing the repair with a Martius flap in anticipation of performing an autologous or allograft sling procedure at another date is one possible approach; alternatively, in rare circumstances, when it is desirable to complete the surgery in one sitting, this could be done at the same time as sling implantation.[9,43,243] Such a situation might arise when a patient's health dictates that the risk:benefit ratio favours a single operation instead of two or, if the patient lives at a great distance from the treatment centre and returning for a second operation would present a major burden.

Bowel perforations during sling surgery are even more uncommon than perforations of other pelvic organs with a reported incidence in 0.005–0.02% of procedures.[132] In a meta-analysis published in 2007, authors reported a mortality rate of 20% in 35 incidences of bowel perforation during sling surgery.[133] Of particular concern is the fact that some patients did not present with any clinical signs of abdominal injury.[102,104,106,132–134,236] Patients' initial complaints were often originally attributed to voiding dysfunction and not until days later, when the patients became seriously ill, was the correct diagnosis made.[237] In five patients the diagnosis of bowel perforation during sling surgery was made only at autopsy.[238]

Voiding dysfunction

The term 'voiding dysfunction' was not clearly defined in the majority of studies in this area and could be interpreted as either voiding symptoms, storage symptoms or both. Some of the terms used include *de novo* or persistent overactive bladder, urgency or urge incontinence, urinary retention and urethral obstruction from SMUS. In addition, secondary voiding problems can arise after sling revision or excision surgeries performed to treat the original complications such as recurrent SUI, dyspareunia, urethral strictures and fistulas.[41,100,111,244] We used our best judgement to assign the authors' intent to one of the categories listed below, but in some instances the author's intent was not clear. For example, one category was listed as "voiding dysfunction requiring surgery",[30] although whether this was a result of urethral obstruction or refractory OAB was not defined. Keeping in mind the caveats listed above, temporary or refractory voiding dysfunction has been reported in 0–33% of patients with a SMUS, and is more common in patients fitted with an RP sling than in those fitted with a TOT sling (REFS 16–23,26,30,33,39,46,47,49–51, 53,54,56,58,59,61–66,68–71,73,74,76,77,79,80,82, 83,86–93,95,97–99,140,145,146,148,151–153,156–164, 166–171,173,174,176–184,186,194–205,207,208, 211,214–218,220,222–229,231–233,235,245–260).

OAB symptoms

The terms used to describe OAB in the studies reviewed included urge or urgency incontinence, urgency, refractory urgency and overactive bladder.[9,261] In addition, the qualifiers persistent or *de novo*[261] were often used. *De novo* OAB, indicating the occurrence of OAB after sling surgery, was reported in 0–48% of patients in various studies (REFS 17,18,20,26,39,46–48,50–53, 55,57–59,61,62,66,67,70,73–77,79,83,87,88,91,92, 96,97,99,140,152,153,155,157,159,161,163,164,166–168, 170–174,177,178,181–186,209,211,213,216–219,222, 224,228,229,231–235,245,249,254,255,259,262–269). Most patients with OAB had symptoms that were said to have resolved within the first month of surgery either spontaneously, or in response to anticholinergics, antibiotics or self-catheterization.[30,194] However, the metrics used to conclude this were inadequate for the task; in fact, the vast majority of studies used no metrics or validated outcome measures at all. When validated instruments were used, they were often, in our judgement, inadequate. For example, the UDI was one of the most common questionnaires used and, as alluded to above, conflates the degree of incontinence with bother.[24] Furthermore, the UDI contains no question that specifically refers to urgency (as opposed to urge incontinence). Approximately two-thirds of women with OAB do not have urge incontinence;[270] thus, use of this instrument is likely to miss two-thirds of the women with urgency or OAB in any series.

In patients with refractory OAB as a SMUS-related complication, a careful search for a remediable underlying aetiology should be conducted. Possible aetiologies include infection, stones, urethral obstruction

and mesh erosion into the bladder or urethra. When such aetiologies are found and treated, the reported success rates are generally high, but the methods used to determine treatment success were generally of poor quality. For example, in reports from two studies of endoscopic laser ablation of eroded mesh in patients with OAB the authors reported successful outcomes, but did not use any objective outcome measures.[100,108] Other studies did use validated instruments to quantify outcomes such as the Overactive Bladder Symptom Score, voiding diaries and pad-weight tests.[9] With these caveats in mind, a successful outcome after surgical treatment of these remediable conditions was reported in 28–64% of patients with refractory OAB as a SMUS-related complication.[9,30,43,85]

Urethral obstruction

Urethral obstruction is a urodynamic diagnosis based on high detrusor pressure accompanied by low urine flow rate, although again, no uniform criteria for diagnosing obstruction were used in the papers reviewed. Most investigators simply inferred obstruction based on the temporal relationship between SMUS surgery and voiding symptoms.[271,272] Others used measurements of urine flow rate and post-void residual volume or urodynamics. Urethral obstruction should be suspected in any woman with persistent voiding symptoms (either storage or emptying) after SMUS placement.[9,94,273,274] Obstruction is definitively diagnosed by the findings of high detrusor pressure and low uroflow during urodynamics. Generally, the existence of a normal urine flow rate is thought to exclude the presence of urethral obstruction; however, this is not always the case, as sometimes abnormal urine flow rate can be generated by a strong detrusor contraction or abdominal straining (Figure 1).

Even in the absence of urodynamically confirmed urethral obstruction, sling incision and/or excision can completely resolve refractory voiding (and OAB) symptoms. Compression from the sling is by far the most common cause of urethral obstruction, and at least one case of urethral stricture accompanied by urethral erosion has been reported.[9] The incidence of urethral obstruction requiring surgical intervention ranges from 0% to 8.9% in patients fitted with RP slings and from 0% to 21.3% for those with TOT slings (REFS 17,18,20,21,23,26,30,46–48, 50–56,58,59,61–64,66–69,71,74,77,80–83,86–92,97–99, 148,159,163,166,173,178,180–182,216–218,233,245,250, 253,255,258–260,269). In the largest patient series reported to date, which comprised nearly 190,000 SMUS implantation procedures, and was based on insurance data, a 9-year cumulative rate of sling revision surgery owing to urethral obstruction of 1.3% was reported. Most of this revision surgery occurred in the first few years after the original implantation procedure.[6] In this patient series, however, no mention of the number of patients lost to follow-up monitoring was made, and because investigators only searched for one Current Procedural Terminology (CPT) code (57287) for the sling revision surgery, the actual incidence of revision surgery owing to urethral obstruction was possibly higher. Similarly, a rate of urethrolysis of 3.4% was reported in a cohort of 818 patients fitted with RP slings, although investigators failed to search for 'mesh removal', 'explant' or 'excision'.[275] Owing to incomplete use of these search terms, retrospective studies of databases[6,270] are prone to underestimating the incidence of urethral obstruction requiring surgery.

The reported incidences of urethral obstruction requiring surgery are generally well under 10%. A small number of patients having urethral obstruction in the lost-to-follow-up group could substantially increase the actual overall incidence. In fact, most studies found that 50–75% (sometimes more) of patients undergoing sling revision surgery were treated by a surgeon other than the implanting surgeon.[9,44,276]

Some authors have recommended sling incision or even urethral dilatation for treatment of patients with urethral obstruction, although most authors agree that the entire suburethral portion of the sling should be removed, even if an incision into the wall or urethral lumen is required.[9,40,154,244,261] Whether to remove all of the mesh from RP slings in patients with urethral obstruction depends on multiple factors, including associated pelvic pain, dyspareunia and/or recurrent infections that might be related to retained mesh.[277–280] No meaningful data exist regarding the effectiveness of urethral dilatation; however, based on our clinical experience, we believe that this approach should not be used owing to the possibility of a urethral abrasion that might ultimately lead to erosion.[281] Of course, optical urethrotomy, internal urethrotomy and transurethral incision of urethral strictures should not be done at all except in the rarest of circumstances, for fear of causing iatrogenic urethral exposure.

No clear indications for urethrolysis currently exist; rather, the need for procedures of this type should be considered on a patient-by-patient basis, depending on the degree of scarring and urethral immobility.[282,283] In our judgement, urethrolysis should be considered in patients in whom the proximal urethra feels scarred and immobile during surgery and/or following a finding of limited urethral mobility on a Q-Tip® (Unilever, London, UK) test.

A high, and well documented incidence of recurrent SUI after mesh revision surgery exists, that is reported to range from 10% to 60% of patients who undergo revision surgery.[9,43,78,84,85,94,100,138] For each patient with symptoms of recurrent sphincteric incontinence, a decision needs to be made as to whether or not another anti-incontinence procedure should be considered. Reports of sling revision surgery in patients with sphincteric incontinence are sparse, and often anecdotal; but, if urethral reconstruction is necessary at the time of mesh removal, the AUA guidelines on the surgical management of female SUI[1] state that implantation of another SMUS are contraindicated in these patients. Most authors recommend a wait-and-see approach to management of patients with recurrent SUI after mesh revision surgery, and, as a rule, we agree with this

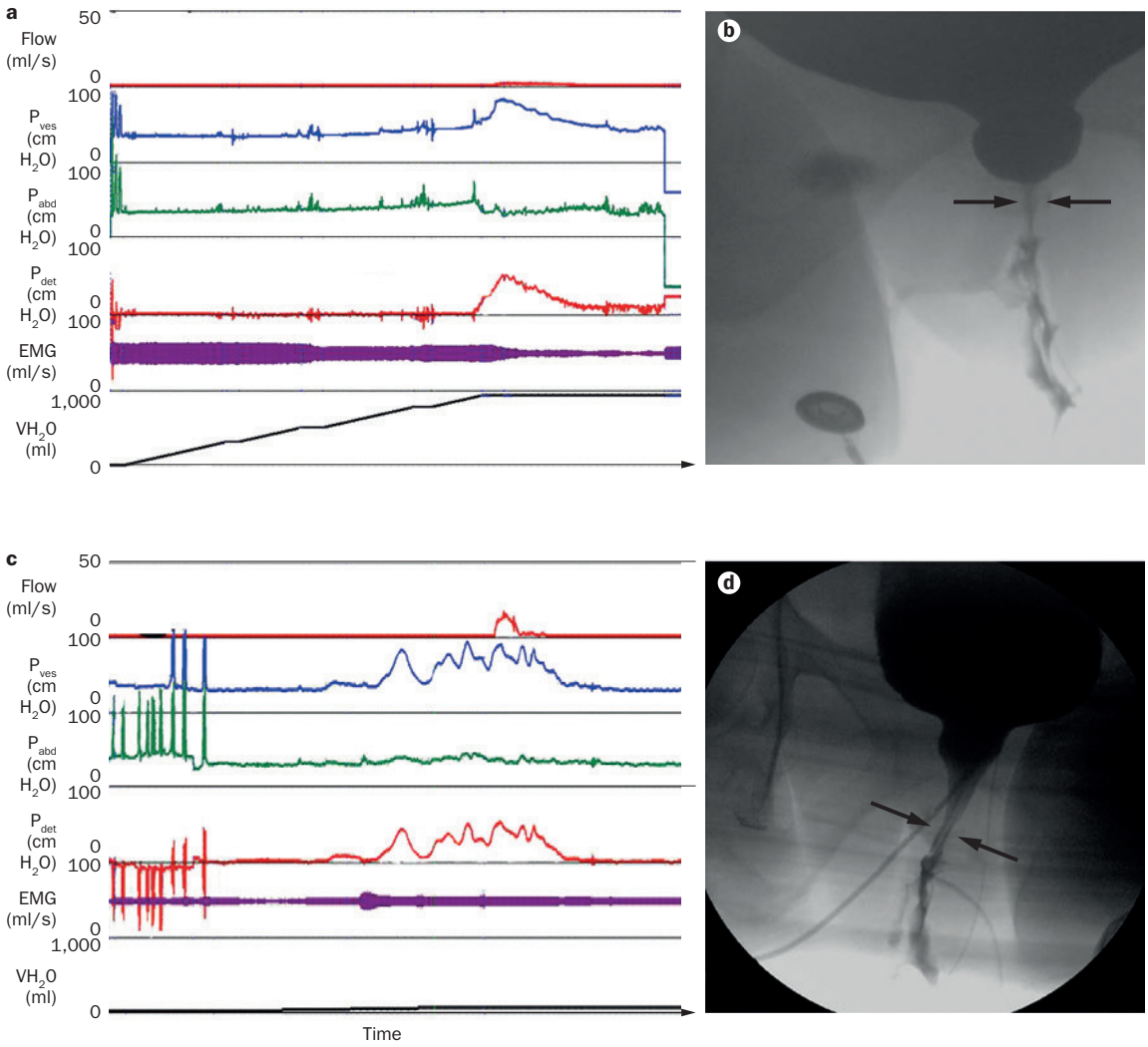


Figure 1 | Identification of urethral obstruction. **a** | Urodynamic trace showing severe urethral obstruction (Blaivas–Groutz nomogram type 2) caused by the presence of a urethral stricture in a 52 year-old woman 4 years postimplantation of a SPARC™ (American Medical Systems, MN, USA) SMUS. Urethral obstruction is confirmed by the presence of strong, sustained detrusor contraction ($P_{det}Q_{max}$ = 56 cm H_2O and Q_{max} = 1 mL/s). **b** | Cystourethrogram confirming the presence of an obstruction owing to the presence of a midurethral stricture (arrows). **c** | Urodynamic trace showing high-flow urethral obstruction in a 52 year-old woman 6 years after midurethral SMUS implantation. Urethral obstruction was confirmed by $P_{det}Q_{max}$ = 56 cm H_2O (Blaivas–Groutz nomogram type 1). Owing to a technical error, infused volume was not recorded on this trace. **d** | Voiding cystourethrogram showing the site of urethral obstruction to be in the distal third of the urethra (arrows). Abbreviations: EMG, electromyogram; P_{abd}, abdominal pressure; P_{det}, detrusor pressure; $P_{det}Q_{max}$, voiding pressure at peak flow; P_{ves}, intravesical pressure; Q_{max}, peak flow; SMUS, synthetic midurethral sling; VH_2O, bladder filling volume.

recommendation. However, data from two published reports contradict this recommendation. A continence rate of 71% was reported in 14 patients who underwent mesh removal after urethral perforations and, in another study, an 82% success rate after revision surgery was reported in 28 patients, of whom 14 had a synchronous autologous sling. In both series a Martius flap was placed between the urethra and sling.[9,43,243] No clear indications exist for conducting synchronous anti-incontinence surgical procedures during mesh excision surgery, although we believe that this approach should be considered whenever extensive damage to the proximal half of the urethra has occurred. Authors of most study reports, however, do not report thoroughly on the outcomes of sling excision surgery.

Mesh erosion, extrusion or exposure

Reports of research in this area of sling complications are typically replete with terminology that conflates the terms erosion, extrusion and exposure; thus, discerning the exact meaning of every author was often impossible. The joint recommendations of the IUGA and ICS[150] provide guidance regarding use of terminology related to SMUS complications, but, in a clinical sense, applying the recommended distinctions is usually not possible in most patients. The IUGA and ICS guidelines define exposure as "a condition of displaying (mesh), revealing, exhibiting, or making accessible for example through the vagina"[150] and extrusion of mesh as "passage gradually out of a body structure or tissue".[150] The guidelines also recommend avoiding use of the term 'erosion' altogether,

but in this Review, we use the terms interchangeably as there is no sound scientific way of making this distinction exists given that the overwhelming majority of authors use this terminology interchangeably. Conceptually, mesh can be seen to protrude through the vaginal wall or into the bladder, urethra or bowel by one of two mechanisms: either it was inadvertently positioned there at the time of surgery or somehow, over the course of time, the mesh gradually worked itself into such a position.

The incidence of mesh sling erosions varies widely between study reports, ranging from 0% to 41% of patients (REFS 16–20,22,26,30,31,39,46–50,52,53, 55–73,75–77,79,81,82,86–90,92,93,95–100,152,153, 155–160,162,164,166–179,181–185,204,207–209, 212–215,217–221,224,225,229,231,233–235,245,247, 252–255,257–259,265,266,268,284–293). The risk factors for sling erosion fall into three main categories: patient factors; mesh characteristics; and intraoperative considerations.[42] With respect to the patient, oestrogen-deficient states, genital atrophy, surgical scarring, concurrent prolapse surgery, type 1 or type 2 diabetes mellitus, steroid use, concurrent anticholinergic use and smoking have been reported as risk factors for sling erosion.[246] Patients ≥75 years of age also had a higher incidence of OAB and recurrent UTI[266] and patients of both younger and older ages (mean ages 55, and 75 years respectively) were variously reported as having adjusted risk factors. Previous pelvic radiation is another obvious risk factor for mesh erosion, but few of these patients undergo sling surgery; thus, this factor did not appear as such in the literature.

Certain types of mesh have a particularly high risk of erosion based on the intrinsic characteristics of the materials they are made from. In a study published in 1997,[190] synthetic materials used for herniorraphy (a type of hernia repair surgery) were categorized based on their composition (synthetic or biological), structure (monofilament or multifilament), pore size (macroporous or microporous) and architecture (knitted or woven). Type I (knitted, monofilament and macroporous polypropylene mesh) is currently considered to be the optimal SMUS mesh material owing to its large pore size (>75 μm), which facilitates infiltration of macrophages and fibroblasts, promotes neovascularity and tissue ingrowth, and minimizes the likelihood of infection. Examples of Type I mesh include VitaMESH™ (Atrium, NH, USA), Marlex® (C.R. Bard, NJ, USA), Prolene® (Ethicon, NJ, USA) and Trelex Natural® mesh (Boston Scientific, MA, USA).

In an attempt to decrease the foreign body responses associated with mesh materials and increase tissue compliance, several manufacturers have designed lightweight meshes of decreased density with smaller fibre diameter and larger pores, with the intention of preventing stiffness, contraction and mesh shrinkage. Several published studies purport some benefit of these new materials in patients requiring inguinal hernia repair; however, all of the studies involved small numbers of patients, with limited follow-up duration, thus precluding any meaningful conclusions.[35,294–300]

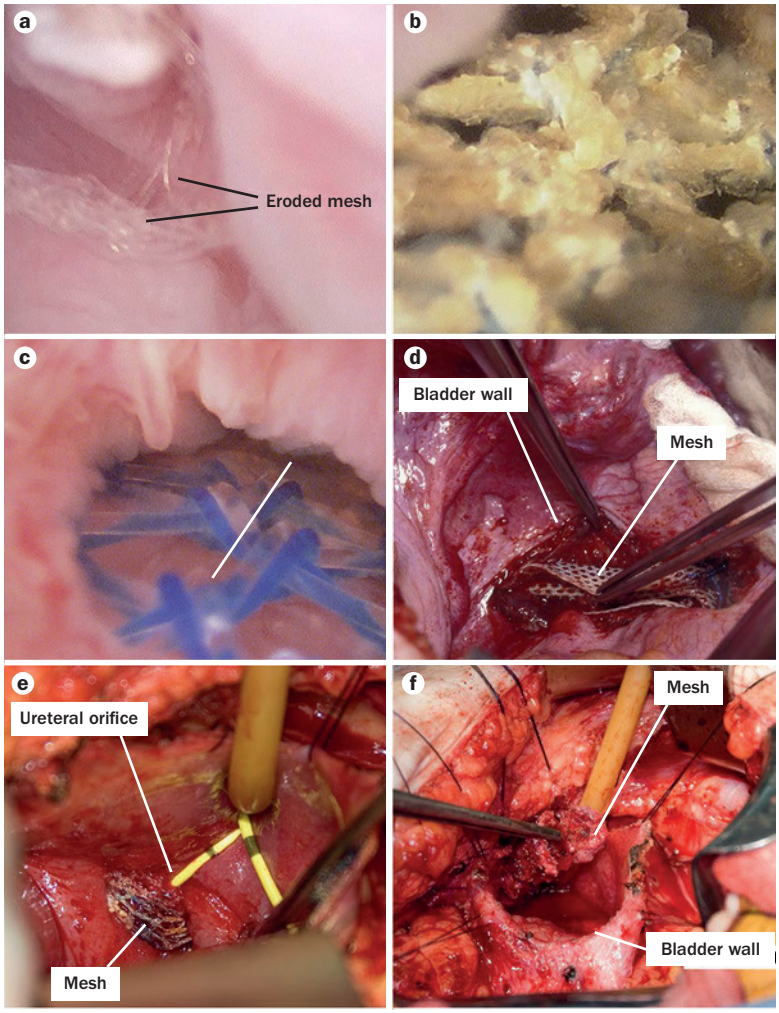
Amid type II mesh (monofilament and microporous) has pores (<10 μm in diameter) that are large enough to allow bacterial infiltration but too small for macrophage infiltration, thus infection is more probable and tissue ingrowth is impeded.[190] Polytetraflouethylene (PTFE, Gore-Tex® W.L. Gore & Associates, DE, USA) is the most common prototype type II mesh. Surgical Membrane Type III multifilament mesh is much denser and stiffer than other types of mesh and has interstices that are <10 μm in diameter with the same negative consequences as those of type II mesh. PTFE mesh (Teflon® DuPont, DE, USA), braided polyethylene terephthalate mesh (Mersilene® Ethicon, NJ, USA), braided polypropylene mesh (Surgipro™ [Covidien, CA, USA] monofilament mesh) and perforated PTFE patch (GORE® MYCROMESH® W.L. Gore & Associates, DE, USA) are examples of type III meshes. Type IV meshes are submicroporous coated biomaterials with pores <1 μm in diameter. SILASTIC® (Dow Corning, MI, USA), Celgard® polypropylene sheeting (Celgard, NC, USA) GORE® PRECLUDE® Pericardial membrane and GORE® PRECLUDE® Dura-substitute (both manufactured by W.L. Gore & Associates, DE, USA) are all type IV meshes. Types II–IV meshes, including PTFE mesh (Amid Type II), silicon-coated polyethylene or polyester (Amid Type IV) and non-knitted, nonwoven mesh such as OBTAPE® and UraTape® (both Mentor–Porges, Le Plessis Robinson, France), have been documented to have a much higher incidence of erosion (16–25%) compared with that of type I meshes (0–10%).[105,109,124,301]

As described previously, bladder, urethral or vaginal perforation during the original surgery increases the risk of subsequent sling erosion by approximately 26-fold.[31] In addition, passage of the trocar through the vaginal, bladder or urethral wall without actually penetrating the lumen might occur, which would result in positioning of the mesh just barely under the surface of the lumen and predisposing it to erosion. This possibility seems likely, although it is currently unproven.

The approach to treatment of sling erosions has been largely empirical, follow-up durations of studies in this area have been short and only a few studies have applied validated outcome measures, especially with respect to the occurrence of other symptoms, such as lower urinary tract symptoms, pain and dyspareunia.[9,44] As discussed previously, recurrent SUI after mesh removal is not uncommon.[9,43,78,84,85,94,100,138] However, synchronous anti-incontinence surgery can be effective in this setting.[43] The authors of this study[40] based their decision to conduct synchronous autologous sling surgery on multiple factors: the location of the urethral injury; preoperative continence status; and the degree of urethral hypermobility. In our series,[9] the success rate (based on PGII score) was 82% after mesh removal, but only half of the patients underwent synchronous autologous sling surgery.[9]

Mesh erosion in the bladder

Bladder erosions are reported to occur in 0–15% of patients fitted with a SMUS (REFS 16–20,22,26,30,46–48,



◀ **Figure 2** | Identification and removal of eroded mesh. **a** | Eroded mesh can be difficult to see during cystoscopy owing to its almost translucent appearance in some patients. **b** | In this erosion, the sling is nearly obscured by the presence of calcium deposits. **c** | Appearance of eroded Amid Type I mesh at urethroscopy. This mesh had no appreciable tissue ingrowth and pulled out of the urethra easily, leaving a small urethrotomy that was closed with a few sutures. **d** | Surgical explantation of eroded silicone mesh. In this case, removing the mesh was relatively easy because it was an Amid type IV mesh, which was encapsulated. **e** | Transvesical explantation of an eroded mesh sling. This type I mesh had tissue ingrowth and required delicate surgery and sharp dissection to enable removal. **f** | Following sharp dissection, the mesh was completely excised from the bladder wall. It coursed over, but did not damage, the ureter. Permission obtained from Fred Govier and Kathleen Kobashi, Virginia Mason Hospital & Seattle Medical Center, Seattle, WA, USA.

50,52,53,55–73,75–77, 79,81,82,86–90,92,93,95–100, 140,152,155–160,164,166–168,170–172,174–177,181, 183–185,207–209,213,215,217–219,221,229,231,233, 234,245,247,253,254,257,258,260,265,266,288–293). Patients with mesh erosions in the bladder usually present with recurrent UTIs, haematuria, bladder stones, incontinence, dyspareunia and pelvic pain; mesh erosions are typically discovered during cystoscopic examinations (Figure 2). Most authors agree on the general treatment principle—all mesh must be removed from the bladder—but the procedures used to do so vary widely. A variety of endoscopic approaches have been used to remove mesh including cutting with scissors and removing the mesh with grasping forceps, transurethral resection of the mesh using monopolar or bipolar current, vaporizing it with a holmium laser[302–310] and even utilizing a small nasal speculum or Metzenbaum scissors passed transurethrally alongside a cystoscope.[311] Results achieved with these surgeries[300–309] have been variable, with some successes followed up for as long as a few years, but the majority of studies had short follow-up durations. Open surgery using a suprapubic or vaginal approach has the advantage of removing all of the intravesical mesh, including mesh that traverses the bladder wall (Figure 2).[9,43,312] Sometimes, partial cystectomy is necessary to remove all the intravesical mesh;[9,10,313] laparoscopic approaches have also been tried.[138] Unfortunately, few studies of patients with mesh erosions in the bladder have sufficiently long follow-up durations or good enough outcome measures to determine the true success rates of these surgeries. Furthermore, all reported successes and failures were compared to the patient's status before the mesh removal surgery, and not before SMUS implantation surgery.

Mesh erosions in the urethra

Urethral erosions are much less common than bladder erosions in patients fitted with a SMUS, with a reported incidence of 0–2.6%.[46,61,100,176] Urethral strictures caused by mesh erosions are even rarer than urethral erosions.[314] A number of different aetiologies of urethral erosion have been postulated, including surgical transgressions (excessive sling tension, unrecognized urethral perforation and passage of the sling through the urethral wall), urethral dilatation,[281] postoperative contraction of the sling,[315] infection, inflammation and immunological reactions.[33,315–319] Treatment of urethral erosions might be as simple as excision of the mesh, which sometimes pulls easily out of the urethra, (Figure 2) or can involve extensive surgical excision of the mesh with part of the urethral wall requiring urethral reconstruction and a Martius flap (Figure 3).[320]

Vaginal mesh erosion, extrusion or exposure

Vaginal mesh erosion, extrusion or exposure has been reported in 0–19% of patients with a SMUS (0–11% of patients with an RP sling and 0–19% of patients with a TOT sling, REFS 16–20,22,26,30,31,46,48,50,53,58–60, 62,64,65,67,69,70,72,75–77,79,81,82,86–90,92, 95,97,103,140,156,158,160,164,167,170,175,177,183, 185,218,221,231,233,247,257,260,266,288,291,292). Factors associated with a higher incidence of mesh extrusion include trocar perforation of the vaginal wall during mesh implantation, previous pelvic surgery, diabetes, bleeding complications at the time of surgery, pelvic radiation, smoking, older age and vaginal incision length >2 cm.[31,42,321]

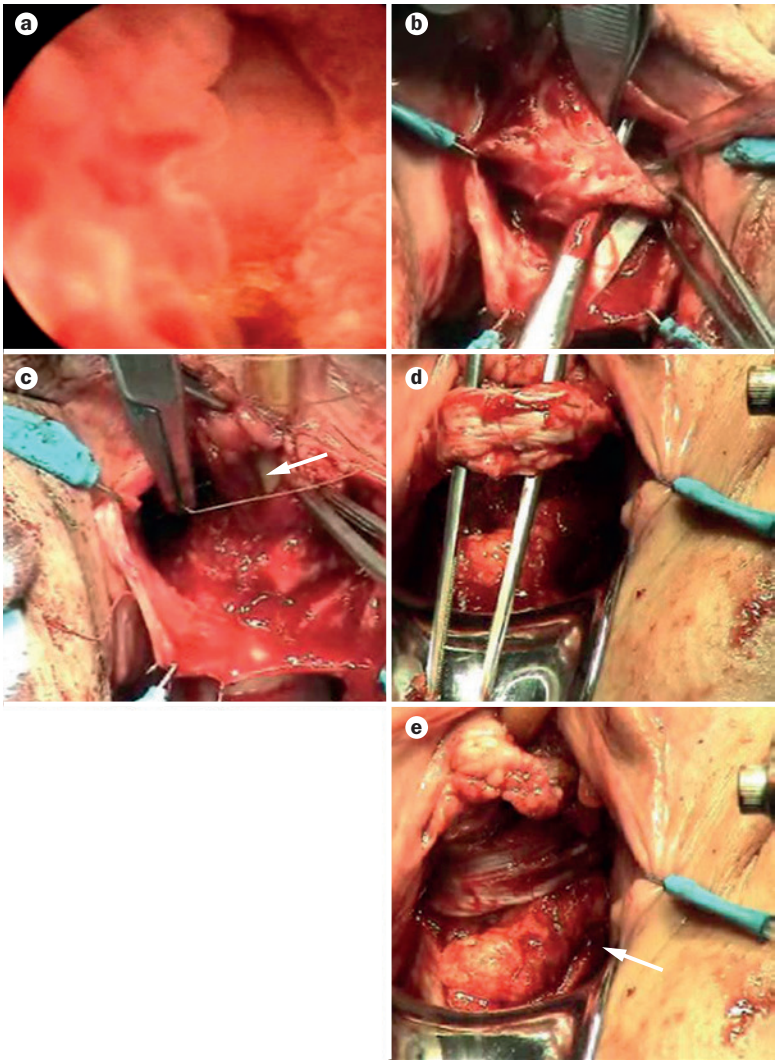


Figure 3 | Identification and removal of Amid type I eroded mesh surrounding the urethra. **a** | Urethroscopic view of urethral erosion. In this case the erosion was very subtle and located in the distal urethra, such erosions are very easy to miss. **b** | Transvaginal dissection and isolation of the mesh shown in image a reveals marked scarring and tissue ingrowth. **c** | Removal required sharp dissection that left a large defect in the urethra (arrow) that required urethral reconstruction, Martius flap and implantation of an autologous fascial sling. **d** | The sling being placed over the urethra. **e** | Creation of a Martius flap (arrow) between the reconstructed urethra and sling, thus repair is completed before vaginal wound closure.

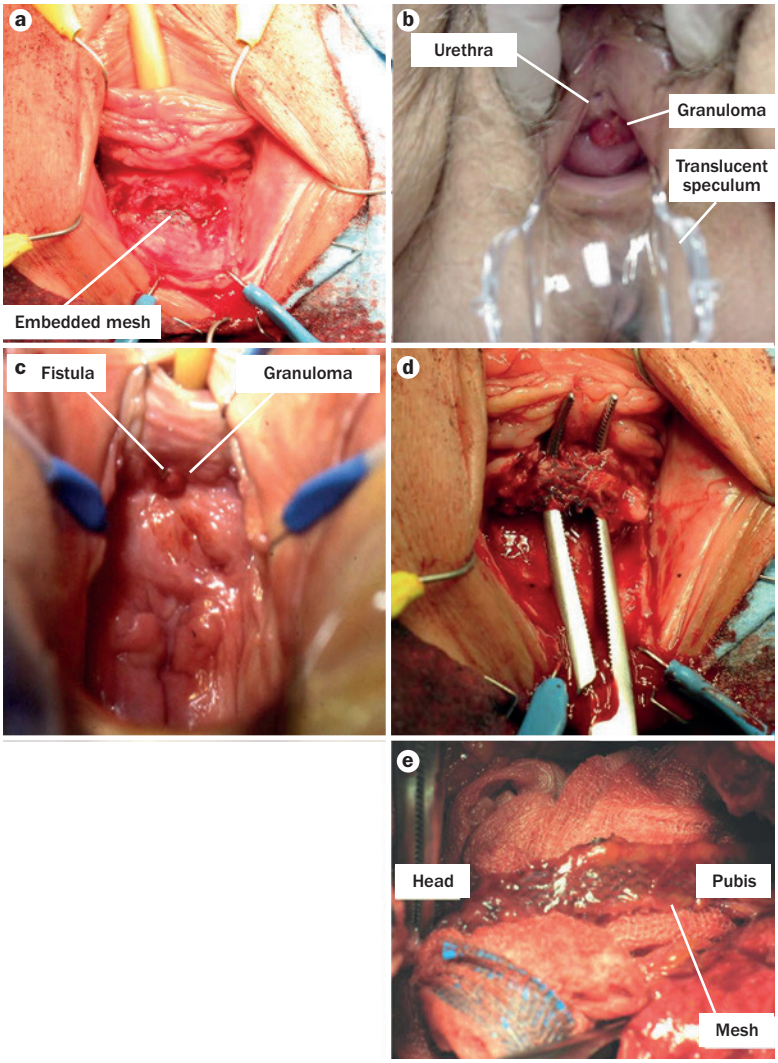
We postulate, based on our clinical experience, several other causes of vaginal mesh exposure including wound dehiscences resulting in exposure of the mesh or implantation of the mesh superficial to the pubocervical fascia so that it lies just beneath the surface.[9] When conditions that favour mesh erosions in the vagina are compounded by local ischaemia, inflammation, foreign body reaction and/or infection, the risk of erosion is likely to be increased. An alternative causative factor has also been suggested —defective wound healing caused by an immunological response to the mesh itself.[33] Vaginal mesh extrusion frequently presents as dyspareunia, vaginal discharge, vaginal bleeding and pain experienced by the sexual partner during vaginal intercourse ("hispareunia").[322] Sometimes asymptomatic extrusions are found during a routine vaginal examination. A diagnosis of vaginal mesh extrusion is typically based on a physical examination —by visual inspection and/or palpation (Figure 4). Most vaginal mesh extrusions occur within the first year of SMUS implantation, although they have been observed in patients as long as 17 years after the original surgery.[16] Some authors report that small areas of mesh exposure can be successfully treated with topical oestrogen,[323] although the results have been mixed.[324] Larger mesh exposures require primary closure of the vaginal wall over the exposed mesh or surgical excision and closure with or without vaginal wall flaps.[30,41–43,45] Mesh exposures of this type are usually reported as minor complications; post-treatment follow up in these patients has been woefully inadequate in most studies.[319,323–325] We did not find sufficient justification in the literature to be able to confidently assess the long-term success of treating these minor exposures. For example, in a retrospective review of nearly 347 complications, the authors found that 73% of patients who initially had nonsurgical treatment for vaginal mesh extrusions ultimately required surgical treatment within 5 years of the original sling surgery.[16,44] In a single-institution study of 79 patients who underwent SMUS implantation, the mean time from SMUS implantation to removal was 2 years with a range of 0–11 years. Despite the fact that mesh erosions can occur >10 years after implantation, most studies report a mean follow-up duration of only 2–23 months.[16,105,261,277,301,312,326]

Mesh erosions in the bowel

Bowel mesh erosions are exceedingly rare and all known patients with bowel erosions have presented with an enterovaginal fistula.[9,327,328] Treatment requires removal of all intra-abdominal mesh and repair or excision of the affected bowel. In our own clinical experience, a patient who had bowel mesh erosion had an associated vesicovaginal fistula and after several unsuccessful reconstructive surgeries required a continent urinary diversion.[9]

Pain

Pain is the most poorly studied complication of SMUS surgery; we found only a few studies that included prospective data collection and/or validated questionnaires assessing pain.[30,79,90,95,152,168,174,229,254] Some investigators used postoperative questionnaires that contained pain questions, but most relied on patients' recall or chart review.[39] In addition, many different descriptors of pain have been reported including vaginal, pelvic, groin, thigh, leg, suprapubic and lower abdominal pain, dyspareunia and "pain, patient self-report."[30] Two different kinds of pain caused by nerve injury have been suggested: centrally mediated hyperalgesia and a peripherally mediated painful hypoalgesia, suggesting the need for mechanism-based classification of neuropathic pain.[329] Most importantly, few of the case studies of patients with SMUS-related pain quantified the severity of this pain,



◀ **Figure 4** | Vaginal complications and removal of SMUS. **a** | View of mesh extrusion into the vagina. This extrusion was both readily visible and appeared palpable on physical examination. **b** | Transvaginal view of eroded mesh obscured by a granuloma. The erosion was neither visible nor palpable. **c** | Transvaginal view of fistula obscured by granuloma. **d** | Transvaginal explantation of an Amid type I RP sling. Note the dense tissue ingrowth and scar that requires sharp dissection in order remove the suburethral portion in its entirety. This portion of the sling felt thickened and stiff. **e** | Retropubic view in the same patient, as shown in image d. The retropubic portion of the mesh after dissection showed fatty tissue ingrowth. This portion was pliable and not scarred. Abbreviations: RP, retropubic; SMUS, synthetic mid-urethral sling.

its character or how the pain affected patients' quality of life.[30,64,82,263] This neglected topic is of the utmost importance and permanently affects "a small cohort of patients whose lives have been unalterably changed for the worse."[40,312]

Pain in patients with a SMUS has been attributed to direct nerve injury during implantation, nerve entrapment, haematoma, infection, chronic inflammation, structural changes to the implanted mesh (shrinkage, stiffening, hardening and/or banding) and scarring.[38,330] Most patients present with pain within the first year of surgery, although some present years later—as late as 8 years postoperatively.[9,110,143] In studies of effectiveness and safety, pain was mostly divided into perioperative pain and pain lasting more than 6 weeks. Perioperative pain has been reported in up to 33% of patients,[252] occurring more frequently after implantation of TOT slings than RP slings,[331] and chronic pain (of any definition) has been reported in 0–31% of patients (REFS 17,18,20,30,39,47,48,53,58,59, 61–63,66,69,70,73,76,79,82,89–91,95,98,99,140,152,155, 159,164,167,168,171–174,177,180–182,185,208,209, 215,223,229,231–233,235,247,250,252,254,255,257,266, 268,290,332,333).

Chronic disabling pain is one of the most common indications for mesh removal, particularly in patients fitted with TOT slings.[9,38,42,44,110,111,277,326] Chronic pelvic pain often contributes to a need for mesh removal; however, these data might not be captured by the approaches used by all investigators. Thus, the reported incidence of pain complications is likely to be falsely low. In comparison with patients with an RP sling, patients with a TOT sling have a higher incidence of persistent pain (32% versus 10%) and dyspareunia (18% versus 3%).[116] This finding is confirmed by a review and meta-analysis in which the rates of chronic groin and leg pain were higher in patients with a TOT sling compared with those of patients with an RP sling (16% versus 6.5%, respectively).[206]

Treatment of persistent pain in patients with a SMUS is particularly challenging and has been entirely empirical and progressive in nature. The treatment approach in these patients typically begins with pain medications and neuromodulatory medications such as carbamazepine, physical therapy or trigger-point injections and culminates with partial or complete mesh excision. Reported success rates of these treatments range from 24% to 100%,[9,40,43,107,277,312,326] but use of validated outcome measures documenting treatment success and long-term follow-up monitoring are both lacking. Furthermore, a number of case studies and series of patients with mesh complications have commented on the lifestyle-altering nature of painful complications in these patients.[9,40,107,312,326]

Fistulas

Urethrovaginal and vesicovaginal fistulas are rare SMUS-related complications, with a reported incidence of <1%.[46,48,66,98,173,178,212,217,334] These fistulas are most frequently associated with bladder or urethral erosion of the sling and patients can present in a variety of ways, and as late as 6 years after the initial surgery.[41,43,44,335–338] Despite their low reported incidence, the possibility of fistulas should be considered when patients present with recurrent incontinence, OAB, pain and/or voiding dysfunction after mesh surgery.[41] Not infrequently, a diagnosis of fistula can be obscured, owing to the presence of adjacent granulation tissue (Figure 4). Concurrent sphincteric incontinence might also confound diagnoses of fistulas,

especially in patients with a urethrovaginal fistula; thus, a careful evaluation should be undertaken to exclude fistula whenever a patient has recurrent incontinence after mesh sling surgery. This evaluation should include a physical examination with a stress test and visual confirmation that leakage is occurring through the urethral meatus as well as cystourethroscopy.[41] Surgical repair of urethral or vesicovaginal fistula requires the complete removal of all involved mesh and possible vaginal reconstruction with tissue flaps.[339] In patients with concomitant sphincteric incontinence, synchronous repair of a urethrovaginal fistula and an autologous fascial sling with a Martius flap interposed between the fistula repair and sling is often an effective treatment.[41,43]

Death

Mortality is the least common SMUS-related complication. In fact, in our literature review we did not find a single case series report that contains a postoperative death of a patient undergoing SMUS implantation surgery; However, In a study of bowel complications of SMUS, published in 2007,[133] 7 deaths from bowel injuries after RP sling implantation were reported, and in 2014 another death after bowel perforation during a retropubic SMUS implantation was published as a case report.[132] Authors of a review of database entries regarding SMUS complications reported 10 deaths owing to bowel injury (six), vascular injury (three) and sepsis (one).[10] Authors of this study[10] suggested that death is an under-reported complication in patients treated with a SMUS.

Complications from mesh removal

Published reports on long-term outcomes of patients after mesh removal surgery are limited. All published studies are retrospective chart or database reviews and substantial heterogeneity exists in terms of both methodology and outcome measures.[9,41,43,44] Most authors of studies in this area commented on the technical difficulties encountered during mesh excision surgery and the fact that many (in some series, most) patients require two or more surgeries; thus, even in the short term, outcomes are often suboptimal.[6,9,40–45] Patients who underwent surgery with a primary indication of urethral obstruction had the highest success rates and those whose primary indication was pain had the least successful outcomes. Perioperative decision making is difficult in these patients and is often highly individualized, mostly based on the surgeon's experience and preferences: whether to attempt removal of all the mesh or just the suburethral or vaginal portions and whether to use a synchronous anti-incontinence or urethral reconstruction procedure.[9] Of note, in patients requiring mesh removal, recurrence of SUI has been reported in 10–60% of individuals.[9,43,78,84,85,94,100,138] An understanding of the possible outcomes of salvage surgery for mesh complications is critical in enabling accurate decisions regarding informed consent for the use of primary mesh surgery; however, few prospective or registry-based studies with published results currently exist that might address this need.[9,44,326]

Mesh–body Interactions

Despite the extensive use of polypropylene mesh dating back to the late 1950s,[340] in a variety of medical procedures, a paucity of data currently exists regarding the fate of this type of mesh once implanted in humans. Almost all of our knowledge of mesh–body interactions is derived from animal studies; explanted material from patients has been largely neglected as a source of information in this area. After >50 years of use, only a few published studies exist in which investigators actually examined histological changes in mesh explants that had been removed from humans.[35,341–343]

Despite this general lack of information, in one study of human explanted mesh samples and pathology records from 102 patients, <50% of explanted transvaginal mesh specimens were examined microscopically; however, when microscopy was performed, results of the microscopic examinations usually did not explain the specific complications experienced by the patients.[253] Several studies have confirmed this finding, noting that the assumption that mesh is widely considered to be biologically inert is based on results of short-term animal experiments without corroborating studies in humans.[342–344] At present, general human tissue interactions with the mesh are known, but we have an incomplete understanding of interactions specific to a mesh material and design as well as the pathophysiology of any complications.

Tissue responses to mesh

Inflammatory reactions

The inflammatory response to implanted mesh is nonspecific, similar to the foreign-body type of reaction initially described in the late 19th century.[345,346] However, only since the 1990s have tissue–implant interactions been studied, and, to date, few reports of the mechanisms involved have been published.[342–344] Immediately after implantation, foreign bodies, including modern implantable polymers, become coated with proteins followed by the appearance of inflammatory cells that migrate into the tissue, owing to the action of inflammatory mediators.[347,348] As in any tissue injury, the acute phase of inflammation is characterized by the appearance of short-lived neutrophils. Neutrophils are replaced within days by macrophages, which persist indefinitely. The initial phagocyte migration towards the foreign body does not seem to be driven by chemoattractants, but is dependent on the proteins, specifically fibrinogen, coating the implanted objects.[347,348] The macrophages then either persist and take on an epithelioid appearance or fuse to form multinucleated giant cells. Macrophage fusion occurs in the presence of certain cytokines, when the foreign object is too large to be phagocytosed by a single cell.[349] The macrophages are recruited in an attempt to destroy the foreign object and are the main component of the granulomatous inflammation triggered by the foreign body. The macrophages secrete an array of substances, such as bioactive lipids, hydrolytic enzymes, reactive oxygen metabolites and mediators of fibroblast proliferation.[350,351] In addition to

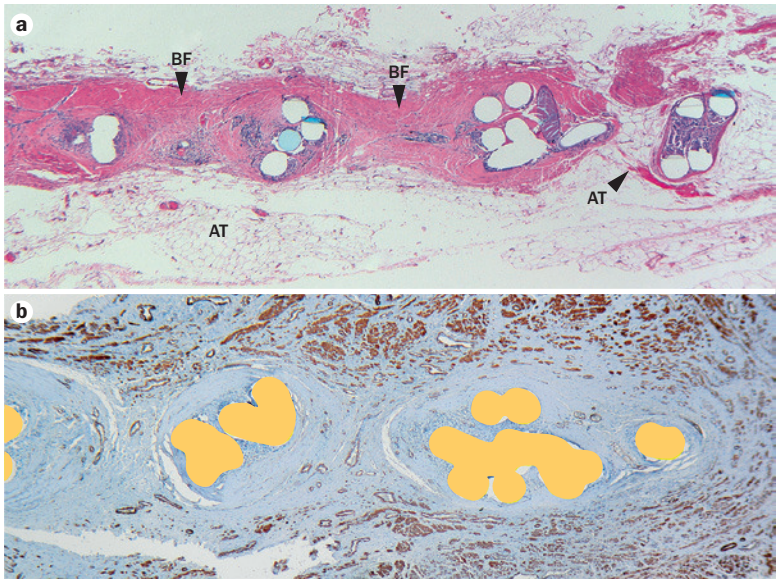


Figure 5 | Scar encapsulating mesh and surrounding pre-existent normal adipose and muscular tissues. **a** | ×2.5 image of a histological section showing a cross-section of mesh filaments as they appear in section, without colouring. Some filaments were labelled blue by the manufacturer. Adipose tissue had been present in the area before mesh placement. Tissue reaction to surgical injury and the mesh generated scar tissue encapsulating the mesh appears as dense pink collagenous tissue. The scar spans, or bridges, across mesh pores, which is termed bridging fibrosis. In this case a terminal pore contains nonscar adipose tissue (arrow with AT). This section has been labelled with a haematoxylin and eosin stain. **b** | ×2.5 image of a histological section showing cross-sections of mesh filaments. Note that the mesh is surrounded by a halo of fibrous tissue separating it from the pre-existent tissue of the vaginal wall, containing smooth muscle. Smooth muscle is labelled with anti α smooth muscle actin (brown), mesh filaments are filled yellow. The blue colour is a haematoxylin background stain. Abbreviations: AT, adipose tissue; BF, bridging fibrosis.

macrophage-mediated effects, a granulomatous reaction includes T lymphocytes as well as a smaller proportion of B lymphocytes and plasma cells. Each mesh filament ultimately becomes surrounded by a sheath of granulomatous inflammation and the entire mesh structure remains chronically inflamed.[342,352–354] Three clinically important aspects of mesh-induced inflammation exist: inflammatory mechanisms of pain, stimulation of fibrosis and polypropylene degradation.

Mesh integration

Mesh integration into the tissue is the result of wound repair mechanisms, which aim to restore tissue continuity. In most mammals after the foetal stage of development, the damaged tissue and void spaces are filled with fibrous, or scar tissue. This fibrous tissue functions as a nonspecific universal repair material or filler. In relation to implanted mesh, the body needs to repair tissue that was damaged during surgery, as well as fill the spaces within the mesh structure. The body also needs to repair the tissue damaged by mesh-associated inflammation.

With implanted mesh, granulomatous tissue inhabits the spaces within the mesh structure, such as the pores and interstices between mesh filaments; however, only provided the spaces are large enough to allow tissue ingrowth.[344] During the weeks after SMUS implantation, collagen deposits accumulate, while the fibroblasts acquire contractile filaments and transform into myofibroblasts. The contractile functions of these myofibroblasts together with reduction of extracellular fluid and collagen crosslinking results in wound contraction;[316,355] the overall aim of wound contraction being to minimize the volume of the maturing scar. In the scar-inhabiting mesh, the contractile forces act on the interlocked mesh–scar composite structure, which results in mesh contraction.[103,316,356] Maturation of the newly generated fibrous tissue is the next step in the repair process. During this maturation stage, collagen becomes increasingly organized and the density of the microvasculature recedes.[355]

Initially, the scar is composed of type III collagen, which is replaced by type I collagen as the scar matures. In the transition from type III to type I collagen, the structure is rearranged into cross-linked sheets that run parallel to tension forces.[355] The repaired area becomes a hypocellular scar that is then slowly remodeled, which can take ≥1 year to complete. Repeated or continuous damage to the tissue can cause the process of repair to be renewed at any stage. Thus, chronic inflammatory conditions can generate a large amount of scar tissue.

With foreign bodies such as mesh, the repair process is complicated by the inflammatory reaction, which is a stimulus for fibrosis. The amount of scar tissue that accumulates is dependent upon counterbalancing processes: stimulation, owing to the presence of a foreign body, and reduction of the scar volume by remodeling. In relation to implanted meshes, fibrous tissue fills the spaces within the mesh structure and surrounds the mesh.[342,343] The tissue then undergoes contraction and remodeling: the stimulus for fibrosis is, therefore, stronger around the mesh filaments and weaker far from the filaments, that is, in the mesh pores. Some larger pores might include fat or other components of normal connective tissue, while the surrounding filaments are fully encapsulated by the scar (Figure 4).[35] Bridging fibrosis can occur in the mesh, where the scar spans or bridges across the pores (Figure 5). Lightweight mesh designs containing pores of several millimetres in diameter have a greater chance of containing normal, nonscar connective tissue in the larger pores of their complex structures.[35,343] By contrast, heavyweight mesh designs, which are currently used for SMUS devices, lead to the development of a continuous scar plate, which encases all mesh filaments and spans across most of the pores (Figure 5).[35,343,357] Scar tissue also provides a connection between the composite mesh–scar structure and the surrounding normal tissue.

The process of healing also includes restoration of interrupted innervation and innervation of newly formed tissue. After mesh implantation the processes of reinnervation and/or neoinnervation are not overly affected by the presence of mesh.[34] Results of a study published in 2014, investigating samples from patients with inguinal hernia showed that the density of nerve branches in the scar encasing the mesh is similar to that of normal tissue

before surgery and marginally, but not significantly, lower than in the scar formed after non-mesh surgery.[34] In addition, nerve branches were observed in the interstices and pores of the mesh, probably growing through the mesh similar to small vessels that were observed to cross the mesh plane.[34] This finding indicates that tissues superficial to the mesh might be at least partially dependent on the through-the-mesh neurovascular supply (Figure 6).

Mesh degradation

The authors of several studies have reported degradation of polypropylene in explanted meshes;[36,341,358–361] however, the question of whether polypropylene degrades *in vivo* has not been fully resolved, despite decades of use.[37,362] Most conclusions of studies in this area were based on the observations of cracking on the exposed surfaces of explanted mesh filaments, which are usually examined using scanning electron microscopy.[351–353,355] The explanted tissue examined in these studies was typically fixed in formalin and had to be separated from the mesh using chemical reagents. Alternative hypotheses emerged that the cracking was either of residual biofilms or, if degradation occurred, it was induced by the formalin or cleaning reagents used. However, other studies demonstrated a similar appearance of polypropylene degradation occurring outside of the human body.[363–365] Before the publication of scanning electron microscopy studies of the mesh surface, authors of an earlier study, published in 1976, assessed the mechanical properties and molecular weight of implanted mesh and concluded that polypropylene degrades *in vivo*.[366] In this study, the investigators placed polypropylene implants with and without antioxidant subcutaneously in hamsters to determine the rate of degradation of the implant. They periodically removed specimens during a 5-month test period and analyzed the samples using infrared spectroscopy and dynamic mechanical testing.[363] The analyses showed that degradation began to occur after only a few days, although several factors suggested that the *in vivo* degradation process was similar to autoxidation that occurs in air or oxygen; in this study, the oxidation process was retarded through the use of an antioxidant.[363] A lack of published studies exists in this area, although the limited evidence suggests that implanted polypropylene undergoes a process of oxidative degradation, in which one of the factors is believed to be oxidative substances generated by macrophages.[366,367]

Effects of mesh on the tissue

Pain

Scar tissue inhabiting the mesh is not simply an inanimate filler, but a living tissue with its own vascular supply, innervation, fluid and acid–base balance mechanisms and immune response.[34,253,368] This tissue is subject to pain through normal mechanisms, caused by specific factors: persistent chronic inflammation, nerve ingrowth, tissue compartmentalization within the mesh and nonphysiological attachments to mobile tissues.

Inflammatory mediators cause hypersensitivity to everyday stimuli that leads to pain in response to touch or on movement and, if the stimulus is sufficiently high, can even lead to pain sensations at rest.[369] As discussed earlier, implantation of polypropylene meshes invariably results in an inflammatory response, which creates an environment capable of decreasing a patient's pain threshold (Figure 7).

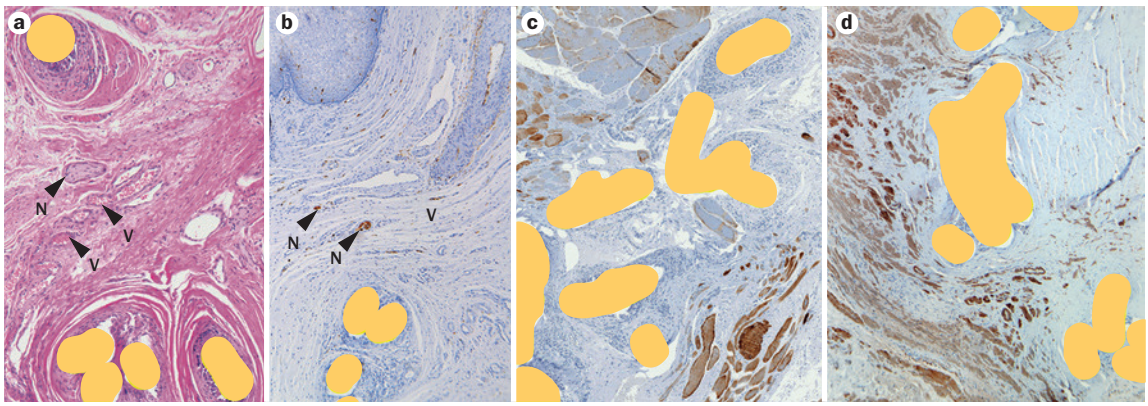


Figure 6 | Tissue interactions with explanted sling materials. **a** | ×10 images of a histological section showing a neurovascular bundle penetrating through a mesh pore. This section has been labelled with a haematoxylin and eosin stain. Cross sections of mesh filaments are filled yellow for demonstration purposes. The neurovascular bundle is within a mesh pore, orientated perpendicular to the mesh plane. **b** | ×10 image of innervation between the mesh and the vaginal mucosa (portions of squamous mucosa in the upper corners). This section has been labelled with S100 stain. The thin layer of superficial innervated tissue is at risk for compression against the mesh during intercourse. **c** | ×10 image of a histological section showing muscle interposition between mesh filaments. This section has been anti-desmin-labelled (brown) to highlight the presence of striated muscle. Interlocked striated muscle is commonly observed in explanted transobturator tapes. **d** | ×10 image of a histological section showing α-smooth-muscle-actin-labelled smooth muscle from the vaginal wall, urethra or urinary bladder surrounding the sling material. Depending on the muscle origin, smooth muscle is likely to interact with mesh during physiological contractions (such as those that occur during urination or intercourse). Abbreviations: N, nerve branch; V, blood vessel.

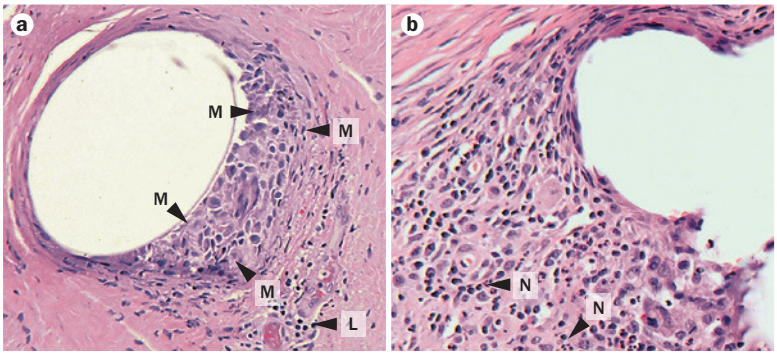


Figure 7 | Inflammatory reaction to the mesh. **a** | ×40 image of a histological section showing a cross-section of mesh filaments surrounded by foreign-body-type inflammation. Epithelioid macrophages (between arrows 'M'), which are the main component of granulomatous inflammation can be observed. A smaller number of lymphocytes ('L') can be seen seen surrounding the mesh filament. This section has been labelled with a haematoxylin and eosin stain. **b** | ×40 image of a histological section showing a cross-section of mesh filaments, characterized by the presence of neutrophils (multiple neutrophils are scattered in the infiltrate, two are labelled 'N' as examples). Acute inflammation is a feature of bacterial infection and is seen in patients with mesh exposure through the vaginal, urethral or bladder mucosa. Abbreviations: L, lymphocytes; M, macrophages; N, neutrophils.

The interlocking and compartmentalized nature is another specific feature of the mesh–scar complex. The ingrown tissue is in a vulnerable position, as it might be subjected to physical compression and distortion within the compartments of mesh pores and folds.[34] The risk of compression might be a result of external forces, such as moving, bending and penile thrusting during intercourse, as well as a result of increased interstitial fluid pressure within the compartments. We have observed evidence of oedema within pores and deformation pockets (folds) of larger mesh devices indicating fluid imbalance within the mesh compartments (Figure 8). Externally, scar connection to the surrounding tissue might cause distortion and pulling during movement. These forces can act on the entire mesh structure, which in a SMUS has a long course compared with that of a hernia patch. This relatively long length of a SMUS might result in multiple sites of scar attachment to the tissues, which, in the case of TOT slings, includes actively contracting striated muscle.[277] These nonphysiological connections are subject to pulling forces that might induce pain, either as a result of muscle contraction or mobility during body movements. Additionally, mesh shrinkage during scar contraction might lead to static tension within and between attached tissues, also contributing to pain.[103]

Many authors have suggested nerve entrapment as a cause of SMUS-related pain. Entrapped nerves have been detected in mesh explants from patients with hernia,[34,35,370] and nerve branches have also been shown to grow into the mesh interstices in up to 90% of explanted mesh samples from patients with hernia.[34,35] Nerve entrapment has also been reported in patients fitted with a transvaginal mesh,[112] although few published studies exist in this area. In our unreported clinical experience of over 100 explanted mesh specimens, nearly all contained nerve branches of variable calibre (Figure 6). Interestingly, in patients undergoing hernia surgery, prophylactic neurectomy is offered as a method to reduce the incidence of pain after mesh repair.[371]

Some patients fitted with a SMUS report pain that is associated with specific movements or activities. The observation of interlocking of the mesh and striated muscle—resulting in muscle contraction and traction on entrapped nerves—offers a plausible hypothesis to explain this phenomenon in patients fitted with TOT slings. We have also observed interposition of smooth muscle, which might contribute to dyspareunia as the vaginal walls contract during intercourse (Figure 6).

Dyspareunia

Direct pressure and a wide range of tissue movement during sexual intercourse both pose additional risks to patients with a SMUS. The vaginal mucosa is one of the most densely innervated parts of the human body. Thus, if this mucosa overlies a stiffened mesh–scar structure, the nerve branches and receptors are subject to compression against the stiffened SMUS during intercourse. In addition, tissue movement on either side of the scar plate can cause traction and distortion of the mesh–scar structure. Findings of a study published in 2010[38] demonstrated the existence of a new complication unique to patients fitted with TOT slings, termed banding, which is a palpable firm scar in the paraurethral folds that was associated with dyspareunia in four of 12 sexually active women who were found to have banding on examination. Unfortunately, no data were presented describing the histopathology of excised tissue that was removed owing to painful banding, although little imagination is required to understand how this effect could cause pain (Figure 9).

Mesh exposure in the vaginal wall

Mesh erosion through the vaginal mucosa can result in a large variety of tissue responses, ranging from no detectable changes to substantial acute inflammation (Figure 7) and even formation of small abscesses. The dense acute inflammation almost always signifies bacterial infection.[372] From our unpublished experience, the site of mesh exposure also has a variable amount of granulated tissue. These changes correlate with the presenting symptoms, which range from no complaints to vaginal discharge, bleeding, dyspareunia and feeling of the exposed edge of the mesh by the sexual partner.

The mechanisms of mesh exposure and/or extrusion through the vaginal wall have not been well studied; however, an approximately 26-fold increase in vaginal and bladder exposure, extrusion or erosion when there had been a vaginal or bladder trocar perforation during the original surgery is known to exist.[31] Other risk factors have also been identified including patients' having undergone prior vaginal surgeries, larger incisions, smoking, diabetes mellitus of either type, pelvic exposure to radiation and older patient age.[96,124,321] The existence of these risk factors suggests that poor healing, lowered antibacterial immunity, insufficient

vascularization, and scarring are all possible causes contributing to mesh exposure. In terms of mesh-specific factors, solid silicone strips or silicone-coated meshes have higher rates of erosion, indicating that choice of material can affect the risk of vaginal mesh exposure.[105,373,374] Compared with other SMUS materials, silicone has limited adhesion to the tissues, which possibly enables more movement of the mesh, or tissue detachment. Patients fitted with a SMUS with a design that incorporates microporous materials with low tissue adherence, such as Gore-Tex® also have higher rates of mesh exposure through the vaginal wall,[375] compared with those of patients fitted with a SMUS that incorporates polypropylene mesh, which has larger pores.[301,356,376] In addition to the lower tissue adherence that enables mesh movement within the tissue, meshes with smaller pores do not allow tissue growth through the mesh. This lack of tissue growth likely interferes with vascularization and innervation of the overlying mucosa, which might lead to dystrophic changes and poor resistance to infection and necrosis.

Results of experiments conducted in animal models showed that the rate of mesh erosion was also dependent on the size of mesh implant, with animals implanted with larger mesh patches having a higher risk of exposure.[356,376] The higher exposure rate of larger mesh implants was likely a result of higher risks of mesh migration. Deformation was associated with the use of larger patches, more interference with vascularization and innervation of the overlying mucosa and the presence of larger volume of inflammation and/or fibrosis. Implantation with a smaller area of mesh might result in less risk of exposure, assuming that exposure is an entirely random event. In our unreported clinical experience of over 100 explanted polypropylene slings, we frequently observed that the exposed part of the explanted mesh was a curled edge piercing through the mucosa, suggesting that edge curling is also a mechanism of vaginal mesh exposure. In addition to the internal properties of a knitted structure, outward pressure of the tissue can act to curl the edge. Interestingly, resection of an exposed part of the mesh, either an edge or a mid-portion, leaves new edges that can also curl and become exposed. In our experience many mesh exposures, SMUS-related or implant-related pelvic organ prolapses recur after trimming of the exposed part.

Mesh migration

Mesh exposure through the vaginal wall seems to have several potential causes. Mesh erosion through the urethral or bladder mucosa reflects mesh migration (or incorrect SMUS placement). Mesh migration through the tissues and into the adjacent organs has been described when used in patients with hernia, in which two types of mesh migration have been suggested to occur: primary migration of unsecured mesh towards areas of least tissue resistance and secondary migration through transanatomical planes. The latter is facilitated by tissue forces acting to displace mesh while remodelling-induced and inflammation-induced tissue resorption enable this movement.[377,378] In patients with SMUS, mesh migration typically occurs into or through the urethral wall, which is a secondary type of migration.[9,10,39,41,326] Excessive tensioning of the sling can act to displace the mesh into the urethra, whereas an inflammatory reaction to a foreign body and the general ability of tissues to remodel under chronic pressures can enable mesh migration. Remnants of partially excised SMUS can potentially migrate in directions other than into the urethra.

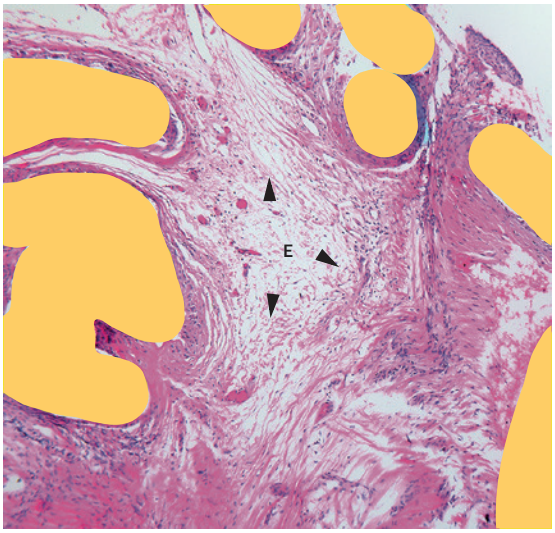


Figure 8 | Oedema within mesh compartments. ×20 image of a histological section showing ooedema in mesh compartments, note separation of collagen and low density of tissue in the area of the oedema (E). Oedema is usually seen in semi-enclosed mesh compartments. Mesh filaments are filled yellow in this image. This section has been labelled with a haematoxylin and eosin stain. Abbreviation: E, oedema

Mesh deformation

Mesh deformation, in which a part of mesh moves from its original or intended position, is related to mesh migration. In an *in vivo* study using white rabbits, Amid type I (Marlex®) meshes were found to be more likely to fold or curl at the edges in comparison to Amid type II meshes (Teflon®).[379] Similar to mesh migration, deformation can be primary, as a result of intraoperative or perioperative folding and edge curling of an unsecured mesh, or secondary, occurring after tissue ingrowth. Secondary wrinkling and folding of the mesh is attributed largely to mesh–scar contraction.[316] For transvaginal applications, folding and bunching of the mesh is frequently observed in patients with pelvic organ prolapse, who are often fitted with large devices, whereas mesh deformation of SMUS devices is typically limited to edge curling (Figure 9).[380] Edge curling of knitted mesh materials has been noticed following their surgical use in patients with hernia, where the edges can be secured by stitching; however, transvaginal devices have all edges unsecured. Narrow sling tapes might also show signs of fraying and curling of the edges when stretched.

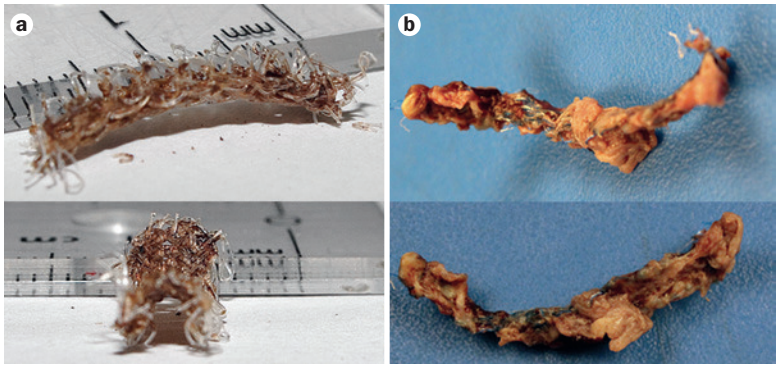


Figure 9 | Curling of the edges of explanted sling materials. **a** | Segment of a sling, which was explanted with very little adherent tissue and a structure that is readily visible. **b** | Segment of a mesh sling, which was excised with adherent tissue remaining attached to the sling material.

To address this risk of sling deformation, SMUS manufacturers have used heat treatment approaches, with variable degree of success.[381] As we note, rotation of a frayed edge towards the mucosa is another possible mechanism by which mucosal exposure of the mesh might take place.

Mesh stiffening

Elasticity and flexibility of knitted meshes is dependent on bending and movement of the mesh filaments. The extent of freedom of movement is often substantially reduced by the ingrowth of collagenous scar tissue. At the same time, the embedded mesh acts to reinforce the scar tissue, thus limiting native flexibility of the scar.[380,382–384] The resultant mesh–scar composite structure is stiffer than the original new mesh. The extent of the resultant increase in stiffness is dependent on mesh design, including the physical characteristics of the material and the amount of induced fibrous scar.[294,316,382–384] For SMUS devices, excessive tightening and connection to the surrounding tissues might limit mobility and add to the structural stiffness. This phenomenon has been observed in the clinic, where it is referred to as 'banding'.[38] Mesh stiffening is likely to occur owing to degradation of polypropylene, as the degraded layer often shows embrittlement.[357–359,361,366] This component of stiffening is expected to increase over time.

Urinary symptoms

SMUS are designed to support the urethra; however, as discussed previously, the amount of pressure can become excessive owing to mesh contraction and reduction of the area of support. A stretched mesh has a reduced width, which, together with edge curling has been described as 'roping' (Figure 9).[385] A stiffened, over-tightened sling, therefore, has limited elasticity and cannot accommodate a full range of changes in tension. SMUS tension changes dynamically during cough, sexual intercourse and other physiological processes, which adds to the static pressure on the urethra. The result is urinary retention and transmigration of the mesh into, or through the urethral wall. Interestingly, mesh removal does not necessarily lead to recurrent SUI.[369,370] This finding suggests that scarring around the mesh, which remains after mesh explantation, is sufficient to maintain continence in some patients.

Polypropylene degradation products

The breakdown of mesh is expected to result in the presence of small molecular complexes and chemical products of degradation, as is the case for any polymerized hydrocarbon. *In vitro* thermal degradation of polypropylene at high temperatures produces an array of organic molecules such as acids, ketones, ethers, aldehydes, alcohols and smaller hydrocarbons.[386] The *in vitro* conditions required for thermal degradation, however, are different to those observed under *in vivo* conditions, and we are not aware of any studies that either simulated body conditions or conducted chemical analysis of explanted tissue. An assumption can be made that, to some extent, any combination of the degradation products detected during thermal or other types of degradation can be produced in the tissue. Additionally, additives used to stabilize the polymer might theoretically leach into the surrounding tissue.

Accumulations of polypropylene degradation products are expected to be confined within the scar capsule and have more local, rather than systemic, effects on the body, owing to their fibrous encapsulation; however, no published studies currently address this point. The degradation products might act as an additional stimulus for the chronic inflammatory response. Accumulation and toxicity of these degradation products might cause tissue damage and contribute to the continuous remodelling around the mesh filaments and extension of fibrosis.[387]

Tumorigenicity

Three cases of cancer that might be associated with implanted polypropylene mesh have been reported in humans. Two patients had squamous cell cancers 6 years and 22 years after mesh hernia repairs, respectively;[388] in addition, an inflammatory myofibroblastic tumour following implantation of an RP sling has also been reported.[384] In the patients who had mesh hernia repairs, both had a complicated clinical course involving chronic mesh exposure and infection.[383] Chronic skin wounds are an established risk factor for squamous cell carcinoma. The one known patient with an RP-sling-related tumour had a myofibroblastic neoplasm with local recurrence potential, which is considered an intermediate state between a benign tumour and sarcoma. Potential risks of tumorigenesis in patients with SMUS include chronic mucosal erosions, chronic inflammation surrounding the mesh and the possible presence of degradation products and polypropylene additives released into the tissue. Mutagenic effects, in general can take many years to accumulate and then a long period to cause a neoplasm. Detecting any oncogenic effects of SMUS implants would require a large cohort of patients with the same type of implant, and these patients would have to be followed up for a sufficiently long period of time, most likely at least 15 years. The long-term use of hernia meshes has not revealed a significant oncogenic risk; however, the

constant introduction of new mesh designs further complicates investigations of mesh-related cancer risks, as these new designs probably vary in terms of the chemical composition of the polypropylene used. In general, based on our knowledge of tumorigenesis, three tissue types might be affected by introduction of a SMUS: epithelium; soft tissue; and lymphocytes, which could result in malignant transformation into carcinoma, sarcoma and lymphoma, respectively.

As described, a small risk of developing squamous cell carcinoma associated with chronic mesh exposure has been reported in patients with hernia meshes.[388] In transvaginal applications of similar materials, chronic erosions might, therefore, increase the risk of squamous cell carcinoma. The importance of concurrent local infections with high-risk variants of human papillomavirus needs to be studied, as these might have a synergistic effect in increasing a patient's cancer risk.

Carcinogenic effects of polypropylene, specifically leading to the development of sarcomas, have been studied in animal models. In rodents, implantation with flat polypropylene plates resulted in higher tumorigenicity than placement of porous materials.[389] A study of implanted polypropylene meshes in mice concluded that the risk of carcinogenesis following mesh implantation, if existent, is not immediate; however the follow-up duration of this study was only 2 years.[390] Another group of researchers implanted transponders made of polypropylene into carcinogen-sensitive *p53*$^{\pm}$ transgenic mice and observed development of sarcomas in 10% of animals within 6 months of exposure.[391] Other reports have corroborated these findings.[392–394] The basic research and clinical data suggest that implantation of polypropylene mesh might increase the risk of sarcoma, however if a risk is present in humans it is likely to be very low.

A potential risk of lymphoma needs to be considered in patients with any prosthetic implants, including SMUS, as this effect has been well documented in women with breast implants.[395,396] The exact aetiology of lymphoma owing to breast implants is not presently known, and this increased risk was detected in association with either saline or silicone implants. The increased risk of lymphoma might be related to an inflammatory reaction to the implants, rather than to the material of the devices; therefore, this risk might also be relevant to a large range of other implants that induce inflammatory responses, including SMUS. The large size of breast implants relative to most other implanted materials and the high volume of use for over 30 years might explain why this small, specific risk became detectable. Whether or not the same risk exists in patients with SMUS is currently unknown. In women with breast implants, the average time between implantation and a diagnosis of lymphoma is reported to be 9 years (range 1–32 years).[396]

Conclusion

In the words of the astronomer Carl Sagan—"The absence of evidence is not evidence of absence".[397] With respect to the safety of sling surgery, the lack of good studies about the incidence and severity of SMUS complications is not evidence that these complications are uncommon, nor is it evidence that they are not serious. The effectiveness of synthetic slings remains unchallenged, although, as this Review documents, an increasing body of evidence exists that serious and sometimes lifestyle-altering complications are underreported and underappreciated by doctors and patients alike. The true incidence of SMUS-related complications is unknown, owing, in no small part, to the poor overall quality of the studies. Nevertheless, we have calculated the minimum risks: revision surgery for erosion and obstruction alone, 5.6%; chronic pain, 4.3%; recurrent or persistent SUI, 5.3%; and *de novo* refractory OAB 3.9% (Box 1). These data are not mutually exclusive, although we calculated the overall risk of a serious complication or surgical failure to be 12.5%. We emphasize, though, that these data represent the absolute minimum rate of complications reported in the literature; the actual rate might be considerably higher.

Urologists can and must do better in assessing the long-term safety of SMUS surgery and in developing better methods of monitoring patients and assessing the outcomes of treatment for complications, so that both patients and physicians can be advised of the true risks associated with a SMUS.

Review criteria

A systematic review of the English language literature was performed in August 2014 to investigate the published efficacy, effectiveness and complications of SMUS. The search used a complex search strategy of the Medline database, including medical subject heading (MeSH) and free-text protocols. The MeSH search combined the terms "mid urethral sling", "midurethral sling", "suburethral sling", "urethral sling", "mid urethral slings", "midurethral slings", "suburethral slings", "urethral slings" and "follow-up study". Multiple free-text searches included the terms "Urinar*incont*", "TVT", "tension-free vaginal tape*", "Tension-free vaginal sling*", "Transobturator tape*", "Transobturator sling*", "TVT-obturator", "TVT-O", "TVT secure", "miniarc", "abbrevio", "TOT", "suprapubic arc sling*", "SPARC sling*", "intravaginal slingplasty", "IVS sling", "Raz sling", "Uratape", "ObTAPE", "Prepubic sling*", "Prepubic TVT", "Prepubic tape*", "PelviLace", "Ureter", "Aris", "In-Fast", "Monarc", "I-Stop", "urethral reconstruction", "urethrovaginal fistula", "Obtape", "gortex sling", "silastic sling", "mersilene sling", "marlex sling", "vesicovaginal fistula", "BioArc" individually in the fields title and abstract of the records. Subsequently, the search was limited to only human patients. A total of 995 records were retrieved from Medline, 249 were included. Six of the authors reviewed the full texts to select relevant papers. Discrepancies were solved by open discussion. Once the citations were accrued and the papers read, the bibliographies were cross-checked for any relevant citations that were missed in the initial search, which totalled an additional to 88 articles. Only articles published since 2007 were included in the reporting of complications to update and expand upon a review published in 2008.[334] For the section on mesh–body interactions, the search was not limited to humans nor was there a limit on publication date.

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Author contributions

All authors made a researched data for this article, J.G.B., M.S.B., G.M., R.B. and V.I. contributed to discussions of content, J.G.B., R.S.P., M.S.B., G.M., R.B. and V.I. wrote the manuscript and J.G.B., R.S.P., M.S.B., R.B. and V.I. made a substantial contribution to reviewing and/or editing of this manuscript prior to submission.

ERRATUM

Safety considerations for synthetic sling surgery

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In the legend of Figure 6, Figure 6b was incorrectly labelled in the originally published version of this article. This error has been corrected in the HTML, PDF and print versions of this article.